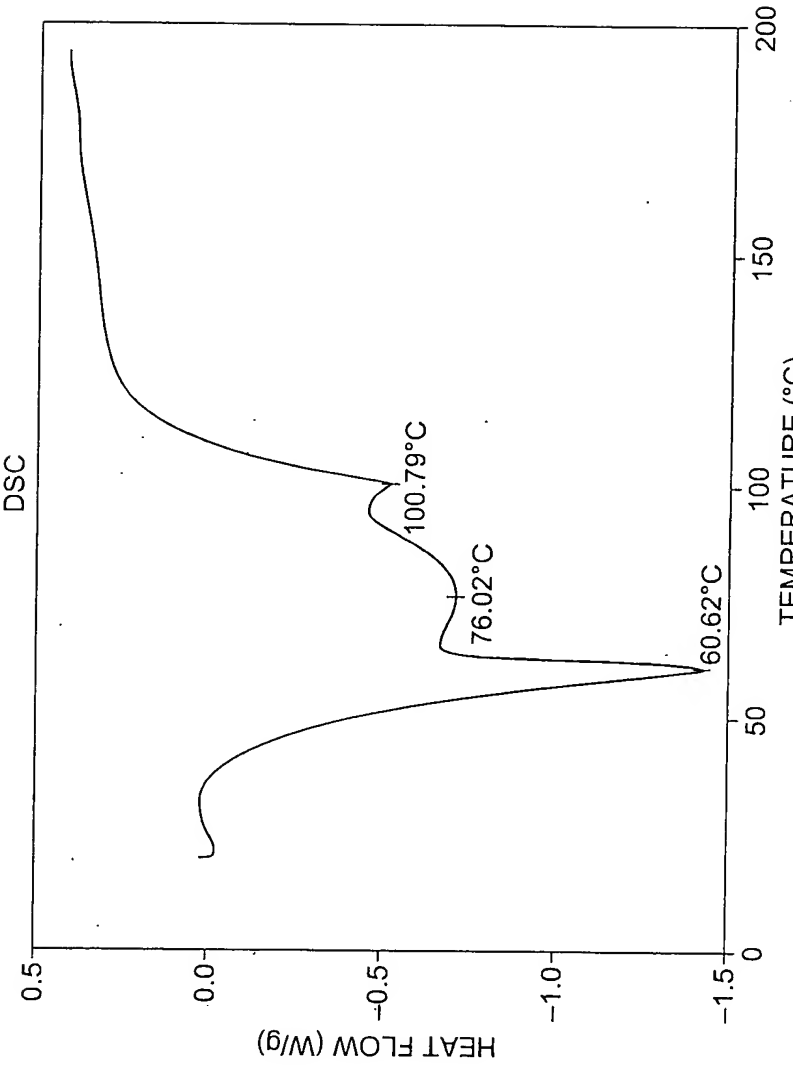


FIG. 1

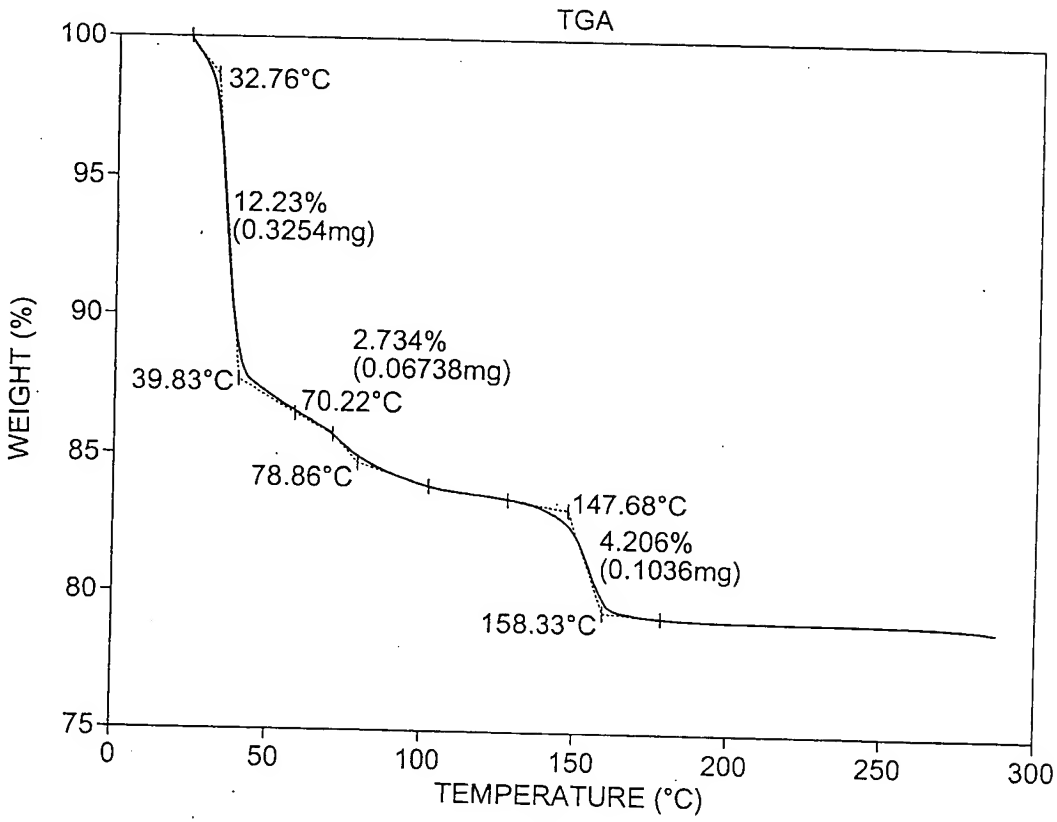

TGA
100
95
90
85
80
75
WEIGHT (%)
32.76°C
12.23%
(0.3254mg)
2.734%
(0.06738mg)
39.83°C
70.22°C
78.86°C
147.68°C
4.206%
(0.1036mg)
158.33°C
0
50
100
150
200
250
300
TEMPERATURE (°C)

FIG. 2

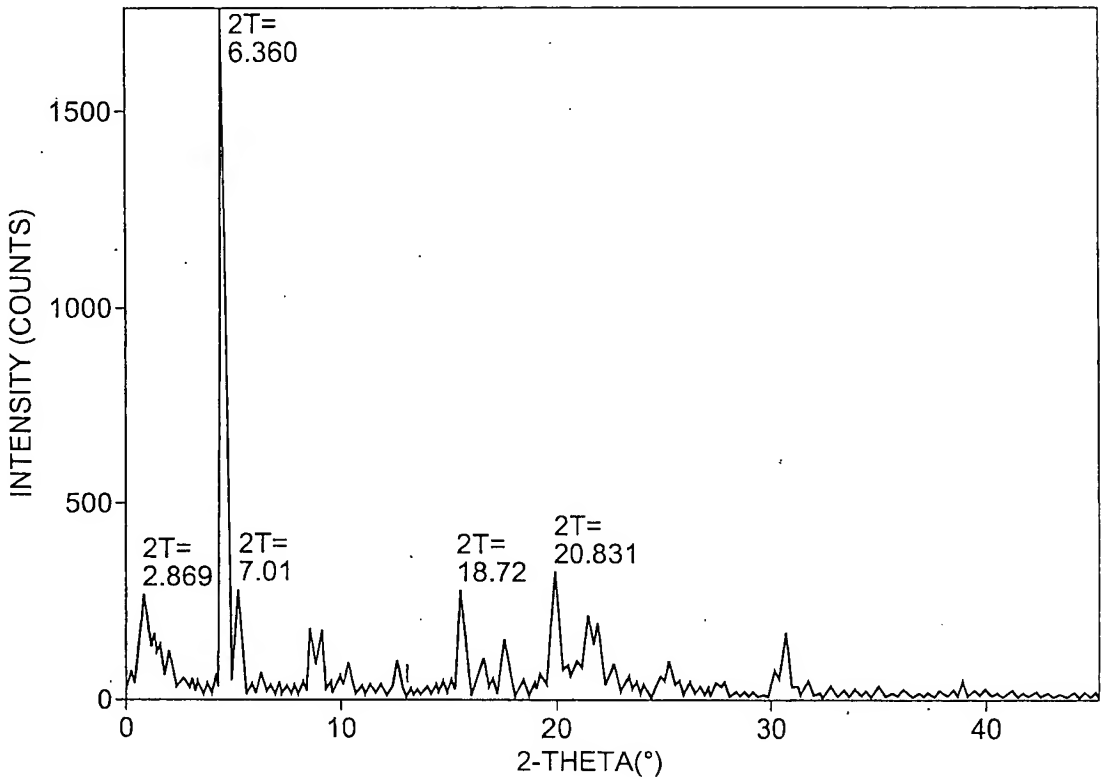

2T=
6.360
1500
1000
500
0
INTENSITY (COUNTS)
2T=
2.869
2T=
7.01
2T=
18.72
2T=
20.831
0
10
20
30
40
2-THETA(°)

FIG. 3

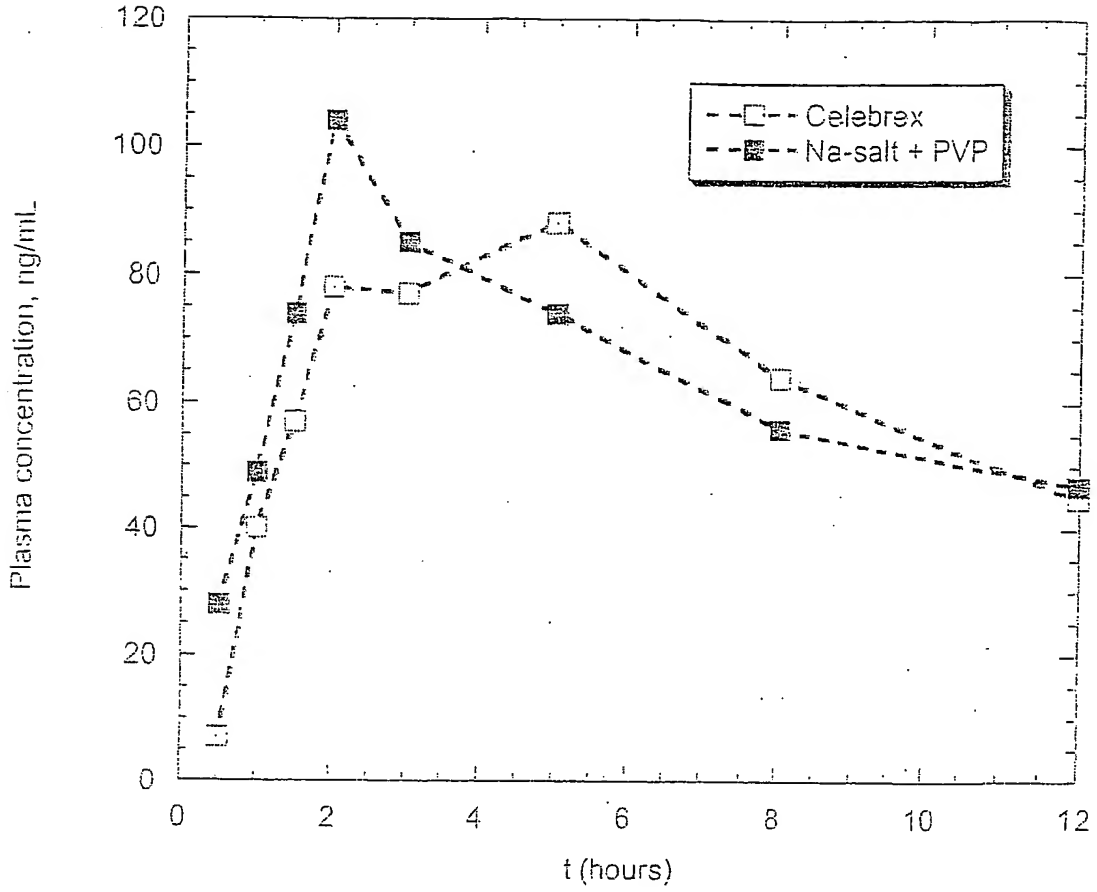

120
100
80
60
40
20
0
0
2
4
6
8
10
12
Plasma concentration, ng/mL
t (hours)
Celebrex
Na-salt + PVP

FIG. 4A

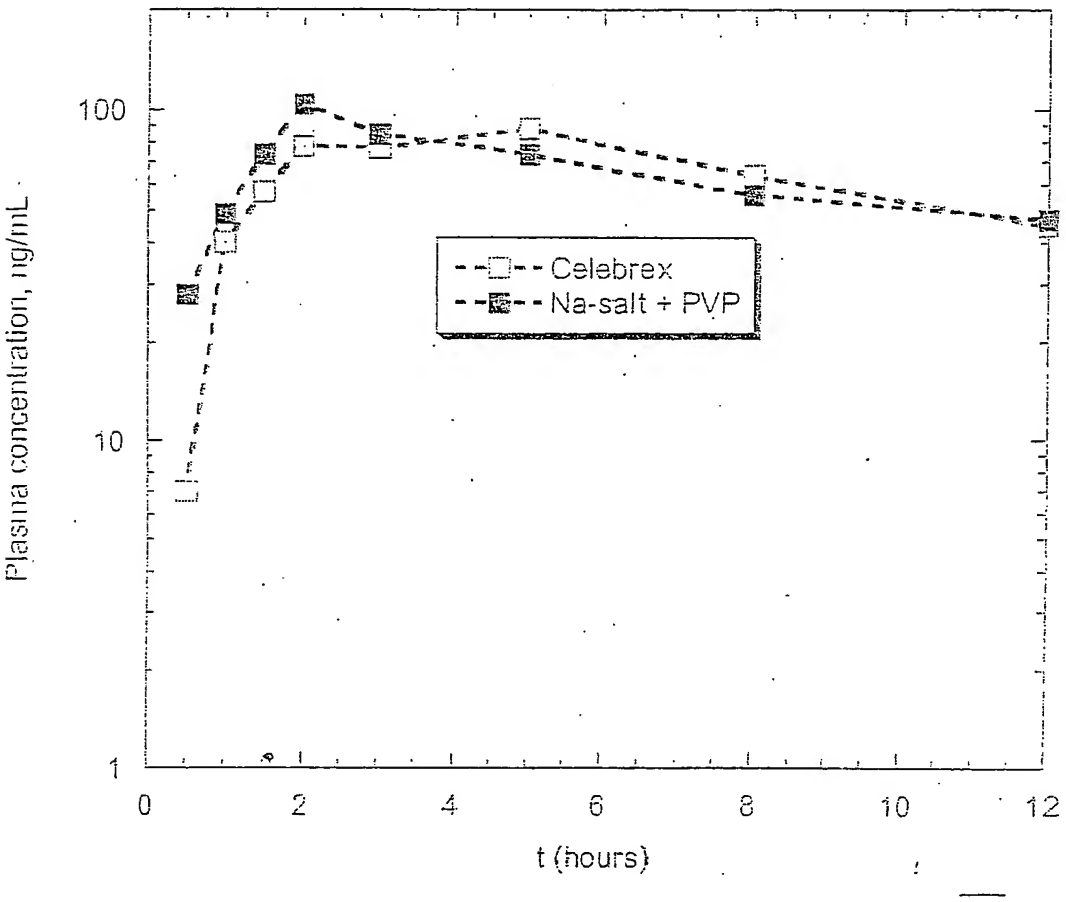

Plasma concentration, ng/mL
100
10
1
0
2
4
6
8
10
12
t (hours)
Celebrex
Na-salt + PVP

FIG. 4B

	Formulation	Dose Level (mg/kg)	C_{max} (ng/mL)	T_{max} (min)	$AUC_{(0-\infty)}$ (ng·hr/mL)	$T_{1/2}$ (hr)	Volume of Distribution at Steady State (mL/kg)	Clearance Rate (mL/hr·kg)	Bioavailability (%)
Mean	Celecoxib IV	1	718	NA	3808	8.21	2498	278	NA
SD		NA	91	NA	933	2.85	590	77	NA
Mean	Celecoxib PO	5.09	654	1.25	7663	9.3	NA	798	40.05
SD		0.050	199	0.88	3119	3.48	NA	317	15.45
Mean	Celecoxib Sodium PO	5.05	2142	0.75	16426	9.0	NA	323	85.80
SD		0.121	569	0.27	4150	2.71	NA	77	7.82

FIG. 5

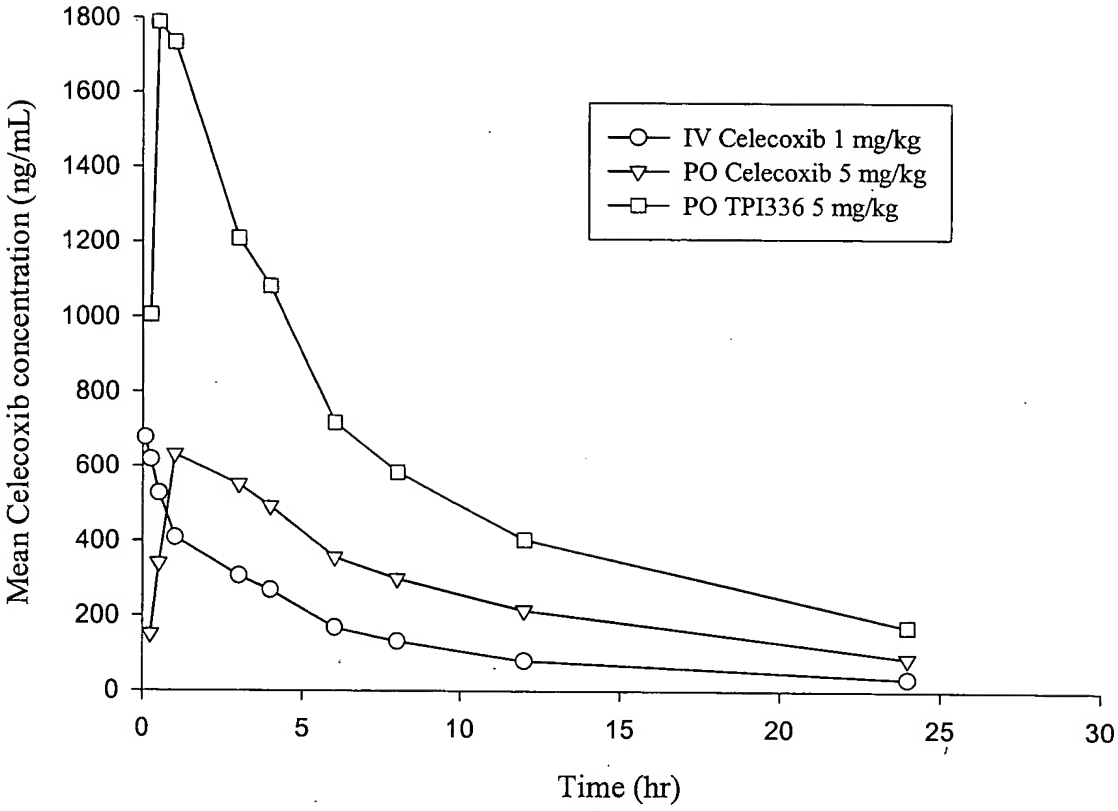
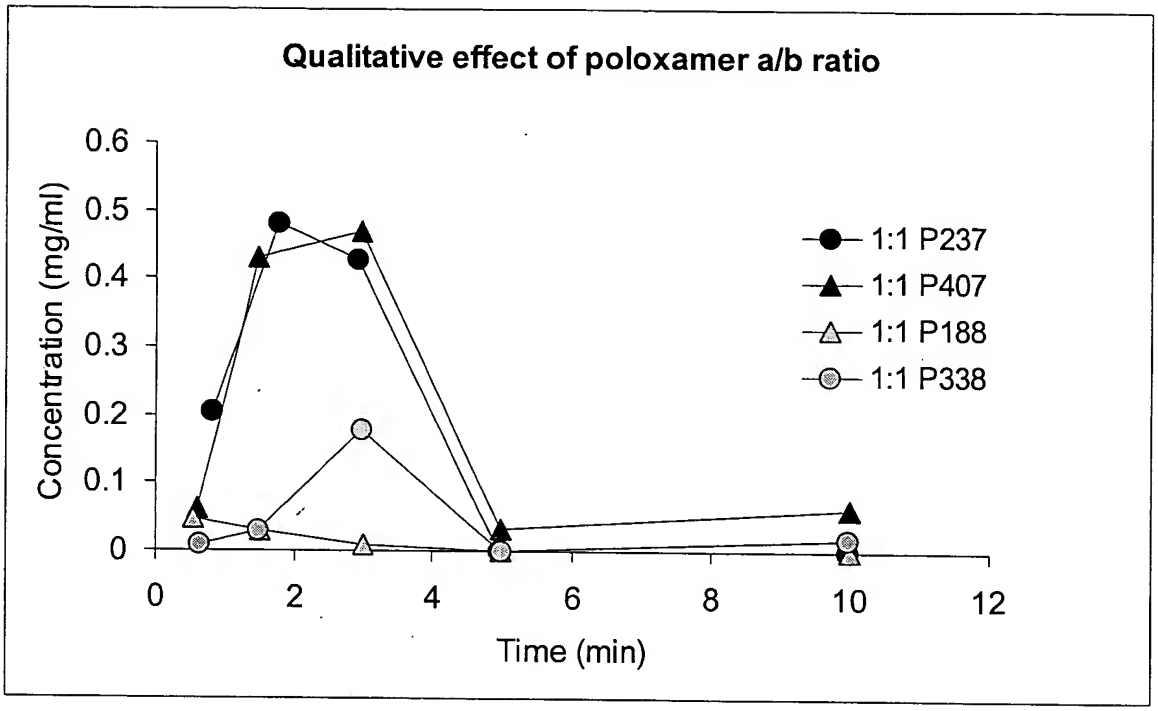

Mean Celecoxib concentration (ng/mL)
1800
1600
1400
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
Time (hr)
IV Celecoxib 1 mg/kg
PO Celecoxib 5 mg/kg
PO TPI336 5 mg/kg

FIGURE 6



Poloxamer	Physical form	a	b	Average molecular weight	Percent a	Percent b	Ratio a/b
124	Liquid	12	20	2090-2360	0.38	0.63	0.60
188	Solid	80	27	7680-9510	0.75	0.25	2.96
[illegible]	[illegible]	64	37	6840-8830	[illegible]	[illegible]	1.73
338	Solid	141	44	12 700-17 400	0.76	0.24	3.20
[illegible]	[illegible]	101	56	9840-14 600	[illegible]	[illegible]	1.80

$HO(C_2H_4O)_a(C_3H_6O)_b(C_2H_4O)_aH$

FIGURE 7

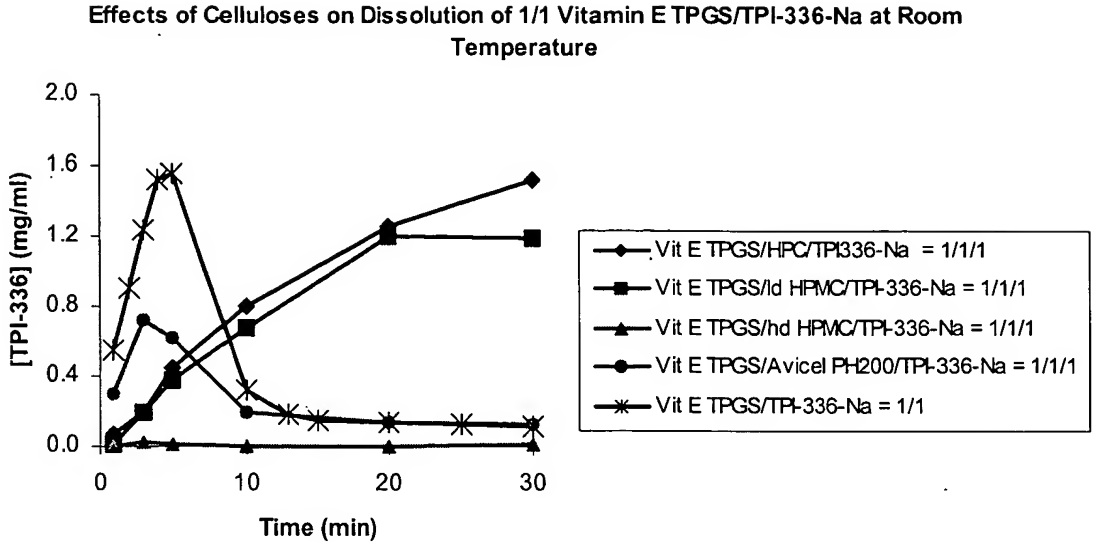


FIGURE 8

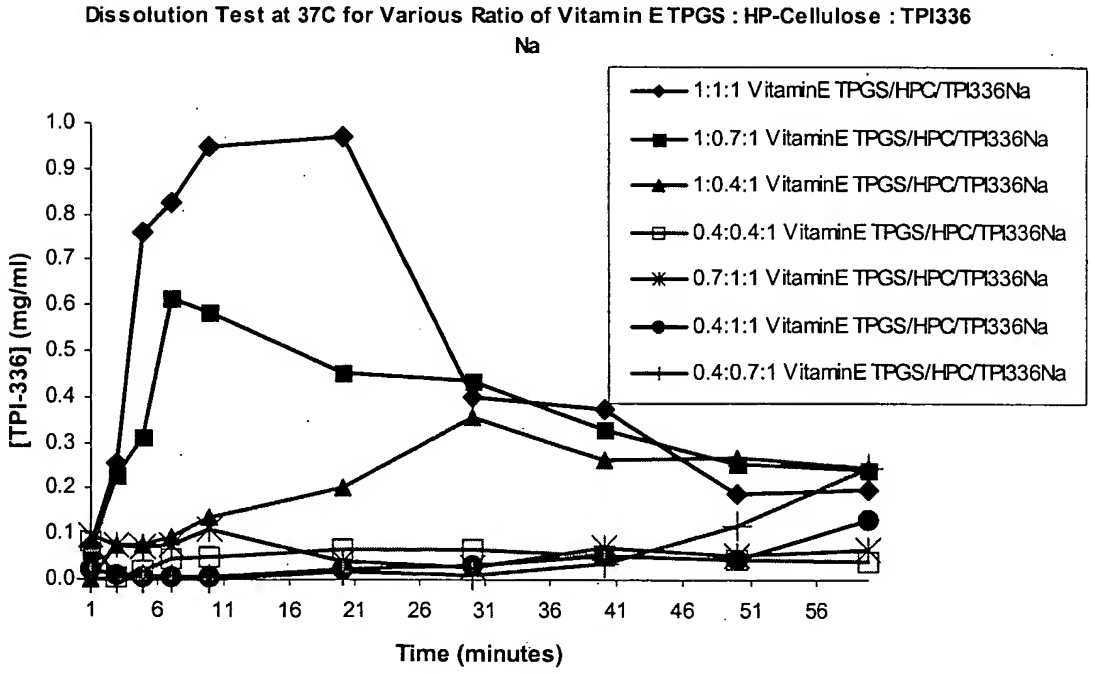


FIGURE 9

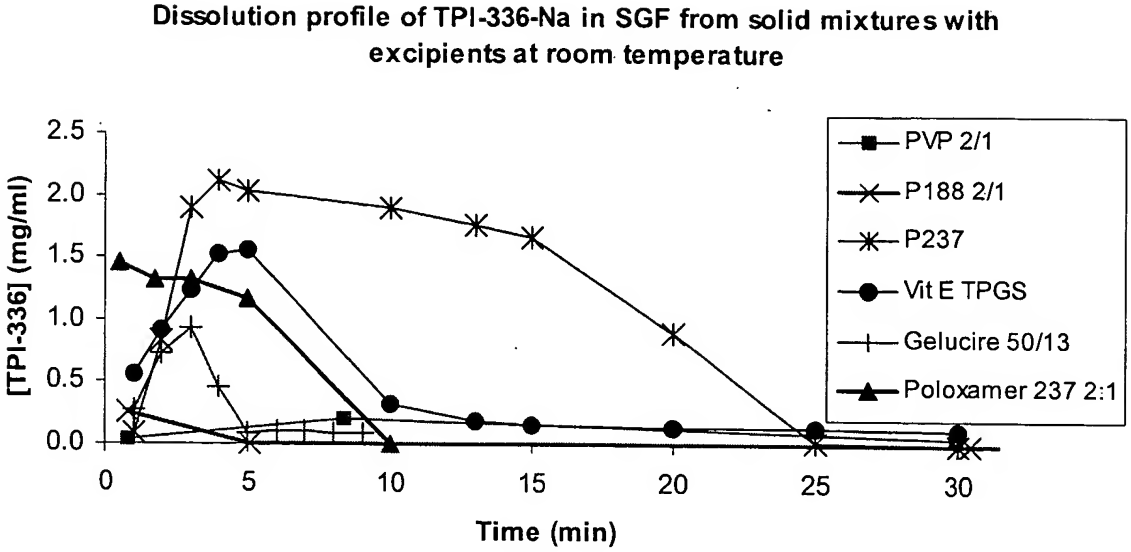


FIGURE 10

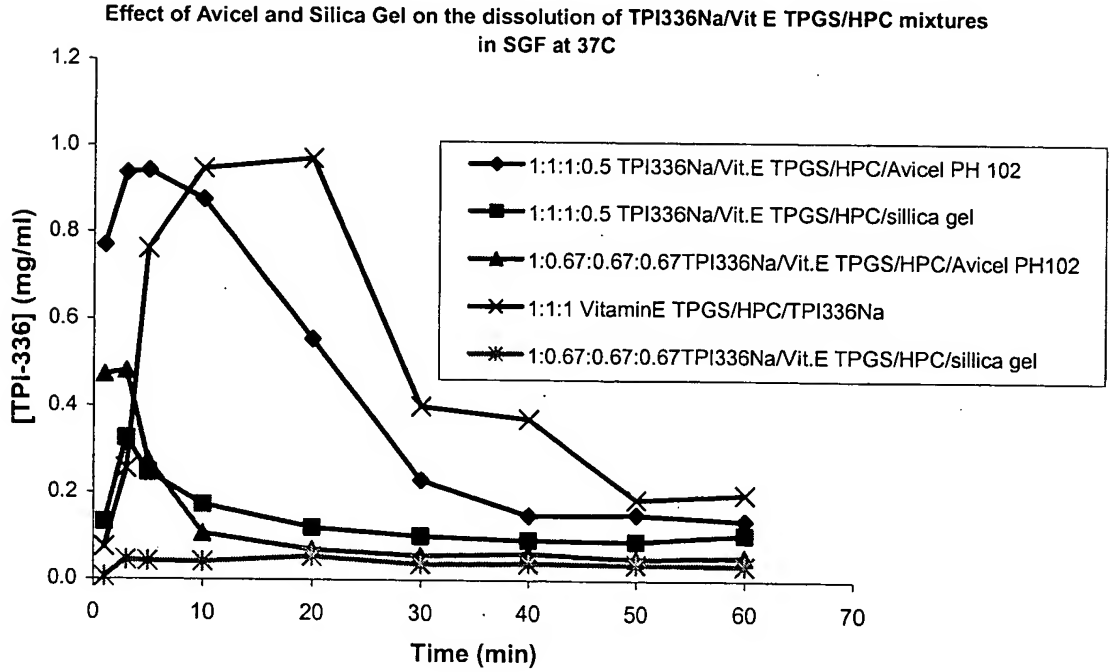


FIGURE 11

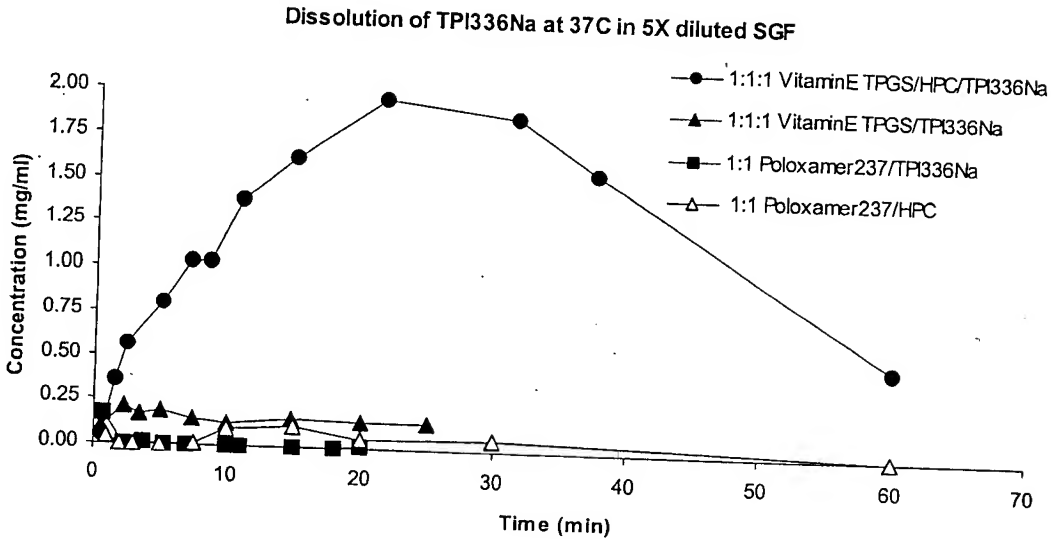

Dissolution of TPI336Na at 37C in 5X diluted SGF
Concentration (mg/ml)
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
0
10
20
30
40
50
60
70
Time (min)
1:1:1 VitaminE TPGS/HPC/TPI336Na
1:1:1 VitaminE TPGS/TPI336Na
1:1 Poloxamer237/TPI336Na
1:1 Poloxamer237/HPC

FIGURE 12

FIGURE 13A

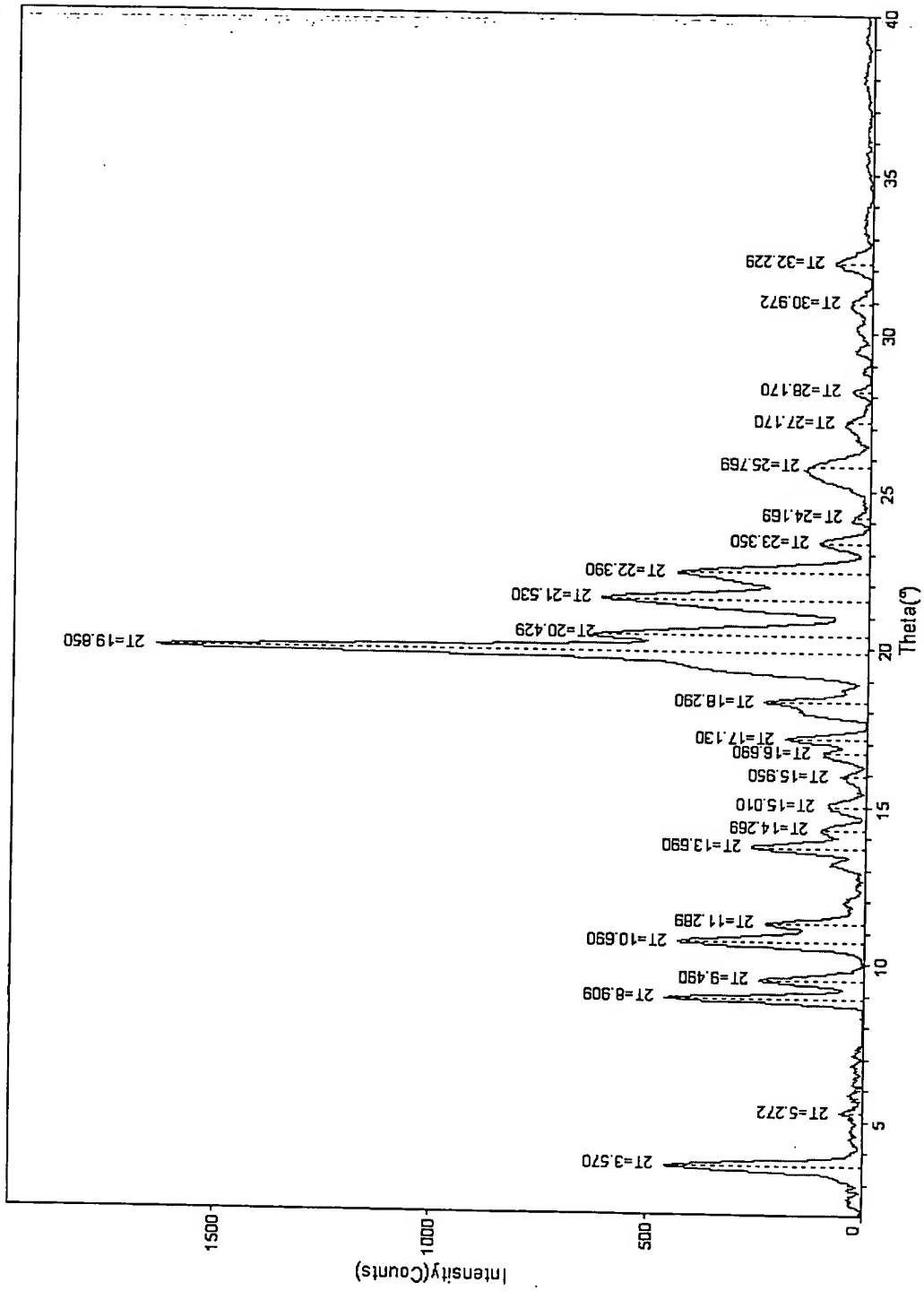
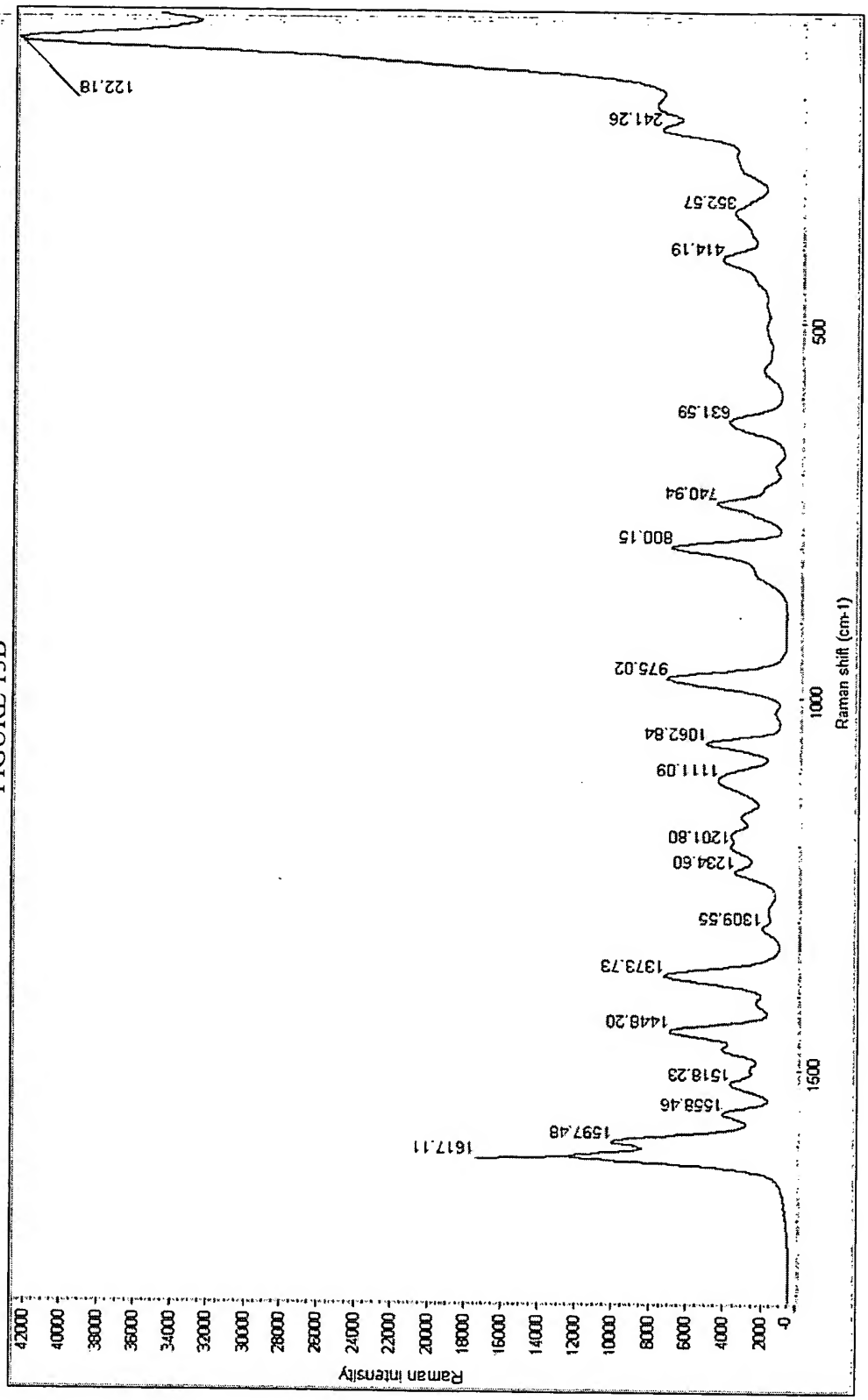

Intensity(Counts)
0
500
1000
1500
Theta(°)
5
10
15
20
25
30
35
40
2T=3.570
2T=5.272
2T=8.909
2T=9.490
2T=10.690
2T=11.289
2T=13.690
2T=14.269
2T=15.010
2T=15.950
2T=16.690
2T=17.130
2T=18.290
2T=19.850
2T=20.429
2T=21.530
2T=22.390
2T=23.350
2T=24.169
2T=25.769
2T=27.170
2T=28.170
2T=30.972
2T=32.229

FIGURE 13B


Raman intensity
Raman shift (cm-1)
122.18
241.26
352.57
414.19
631.59
740.94
800.15
975.02
1062.84
1111.09
1201.80
1234.60
1309.55
1373.73
1448.20
1518.23
1558.46
1597.48
1617.11

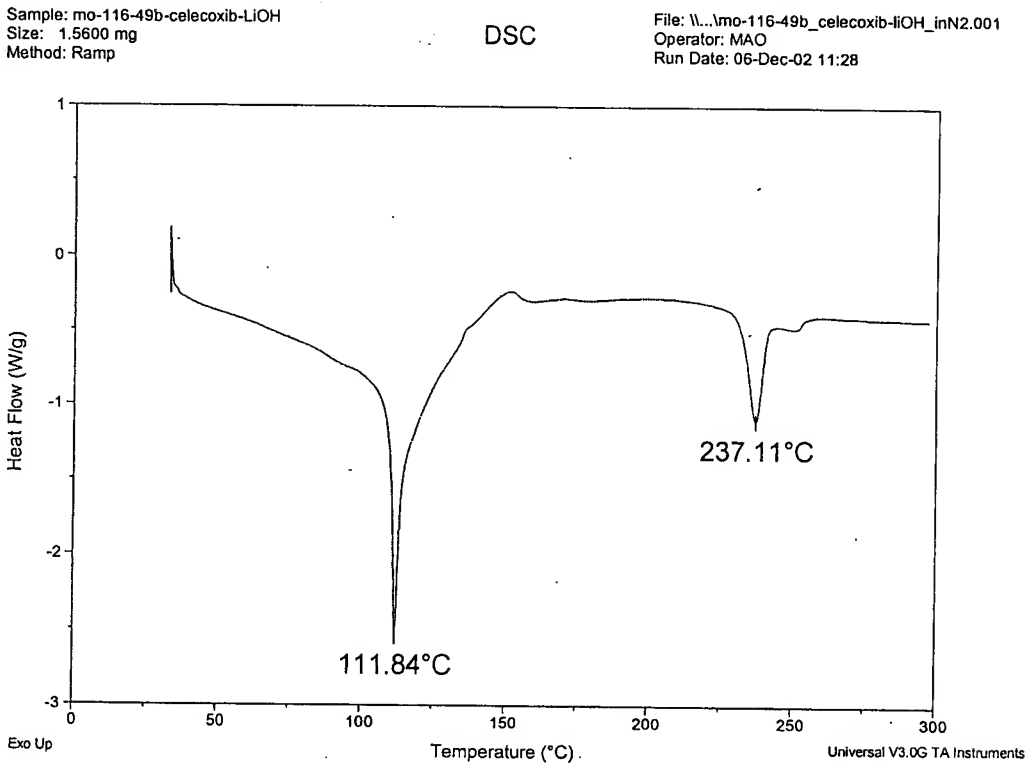

Sample: mo-116-49b-celecoxib-LiOH
Size: 1.5600 mg
Method: Ramp
DSC
File: \\...\mo-116-49b_celecoxib-liOH_inN2.001
Operator: MAO
Run Date: 06-Dec-02 11:28
Heat Flow (W/g)
1
0
-1
-2
-3
237.11°C
111.84°C
0
50
100
150
200
250
300
Exo Up
Temperature (°C)
Universal V3.0G TA Instruments

FIGURE 14

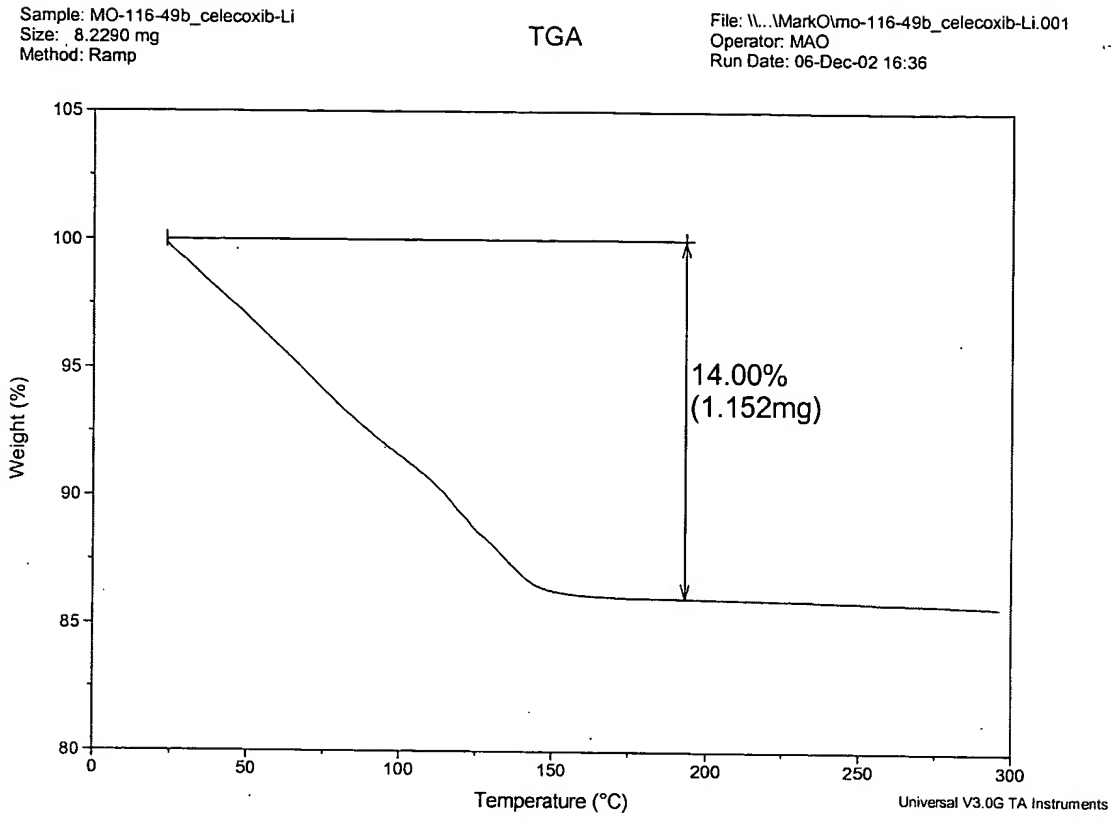

Sample: MO-116-49b_celecoxib-Li
Size: 8.2290 mg
Method: Ramp
TGA
File: \\...\MarkO\mo-116-49b_celecoxib-Li.001
Operator: MAO
Run Date: 06-Dec-02 16:36
105
100
95
90
85
80
Weight (%)
14.00%
(1.152mg)
0
50
100
150
200
250
300
Temperature (°C)
Universal V3.0G TA Instruments

FIGURE 15

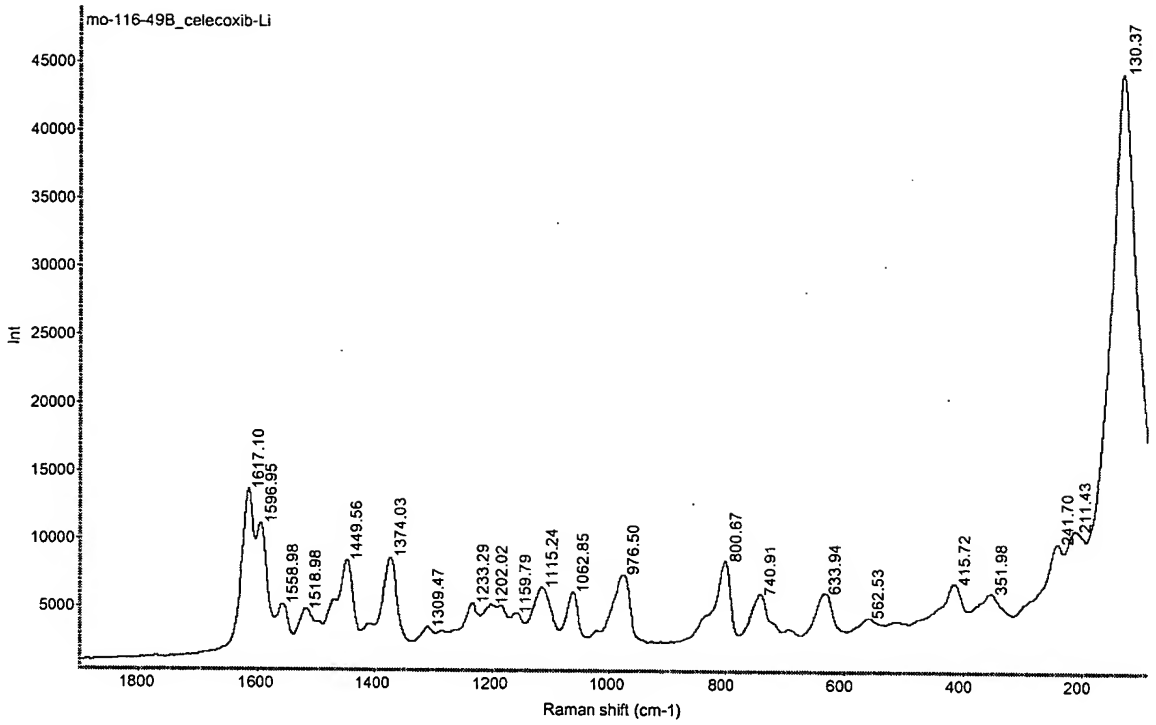


FIGURE 16

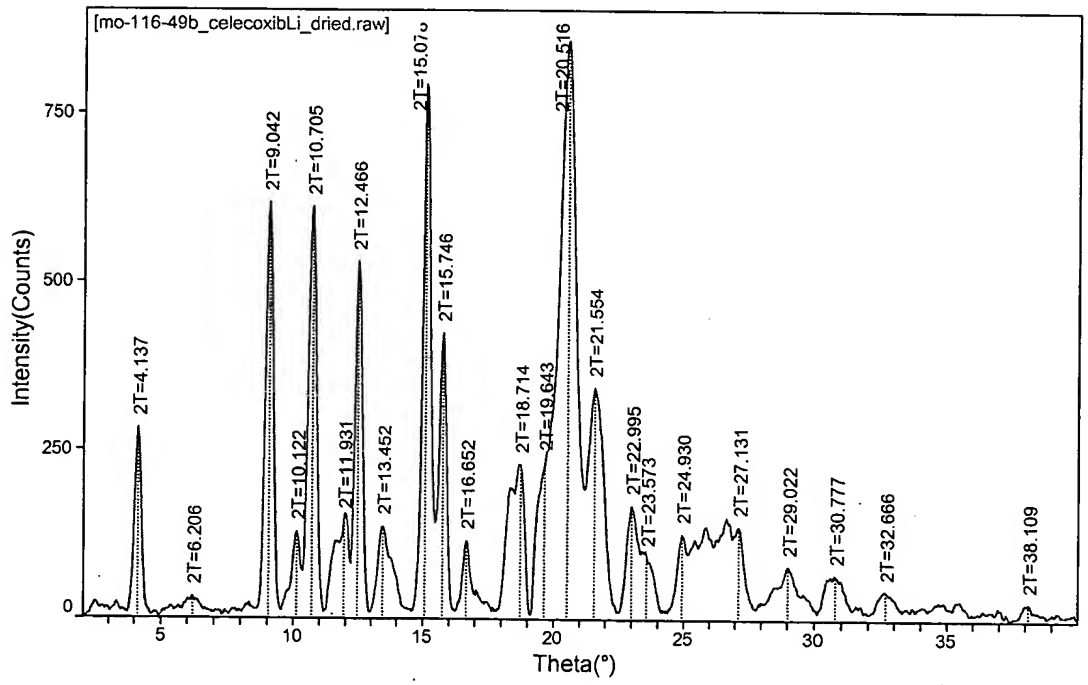


FIGURE 17

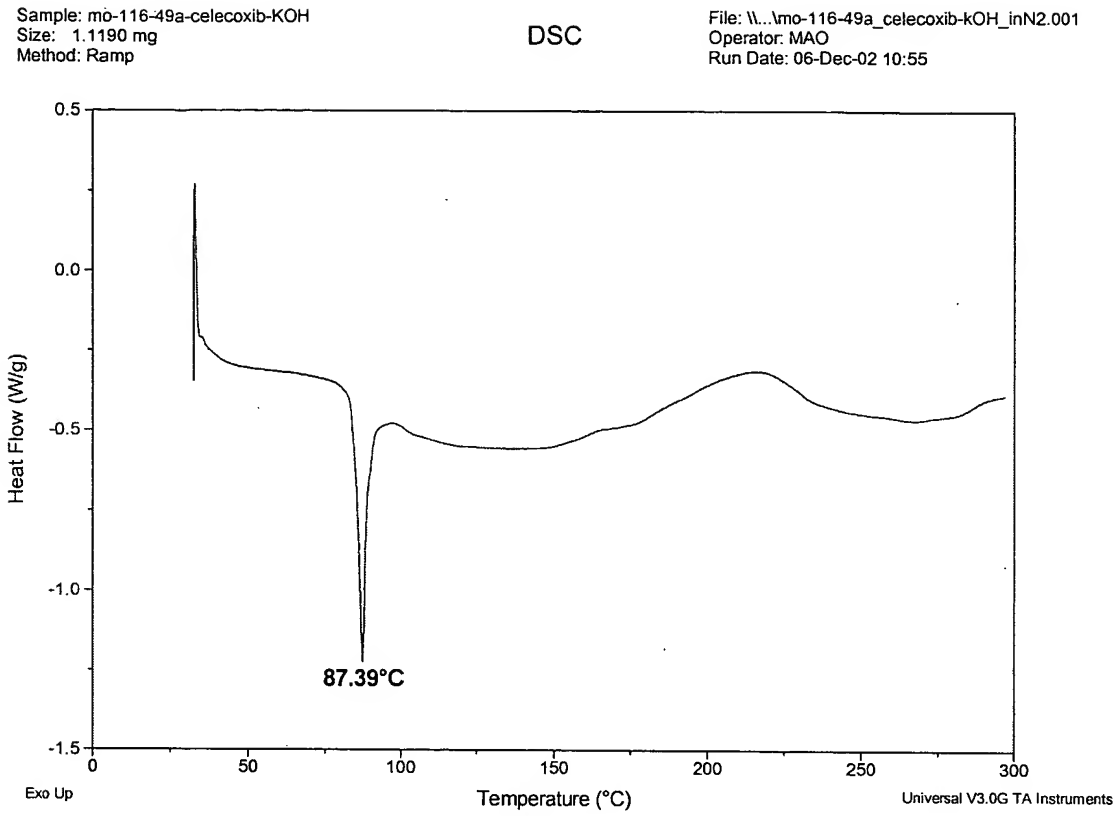

Sample: mo-116-49a-celecoxib-KOH
Size: 1.1190 mg
Method: Ramp
DSC
File: \\...\mo-116-49a_celecoxib-kOH_inN2.001
Operator: MAO
Run Date: 06-Dec-02 10:55
0.5
0.0
-0.5
-1.0
-1.5
Heat Flow (W/g)
87.39°C
0
50
100
150
200
250
300
Exo Up
Temperature (°C)
Universal V3.0G TA Instruments

FIGURE 18

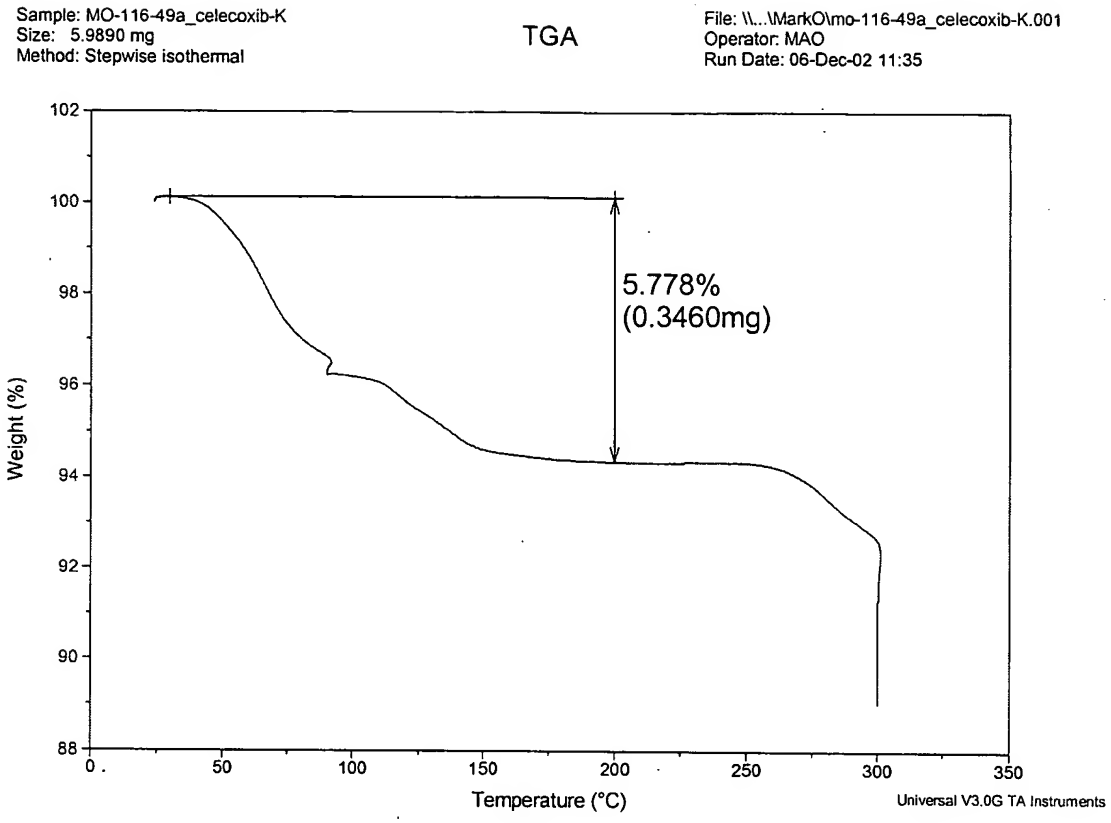

Sample: MO-116-49a_celecoxib-K
Size: 5.9890 mg
Method: Stepwise isothermal
TGA
File: \\...\MarkO\mo-116-49a_celecoxib-K.001
Operator: MAO
Run Date: 06-Dec-02 11:35
5.778%
(0.3460mg)
Weight (%)
Temperature (°C)
Universal V3.0G TA Instruments

FIGURE 19

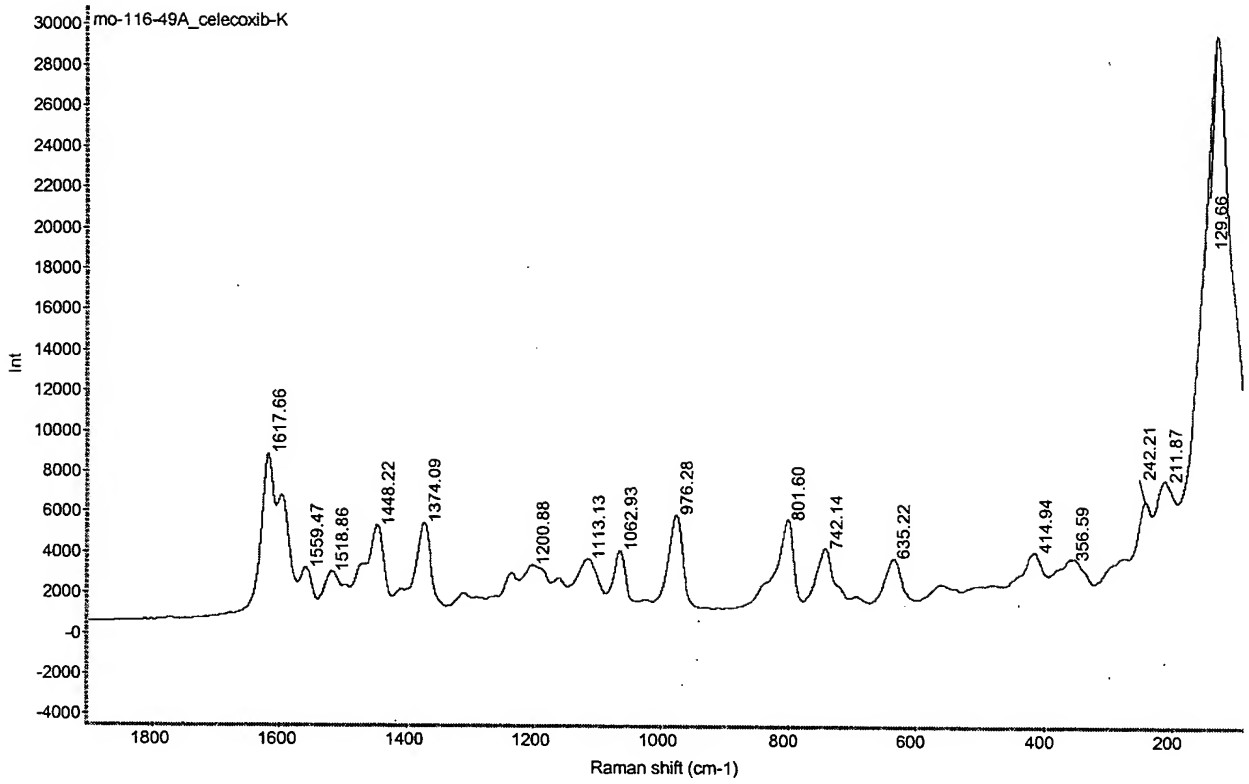


FIGURE 20

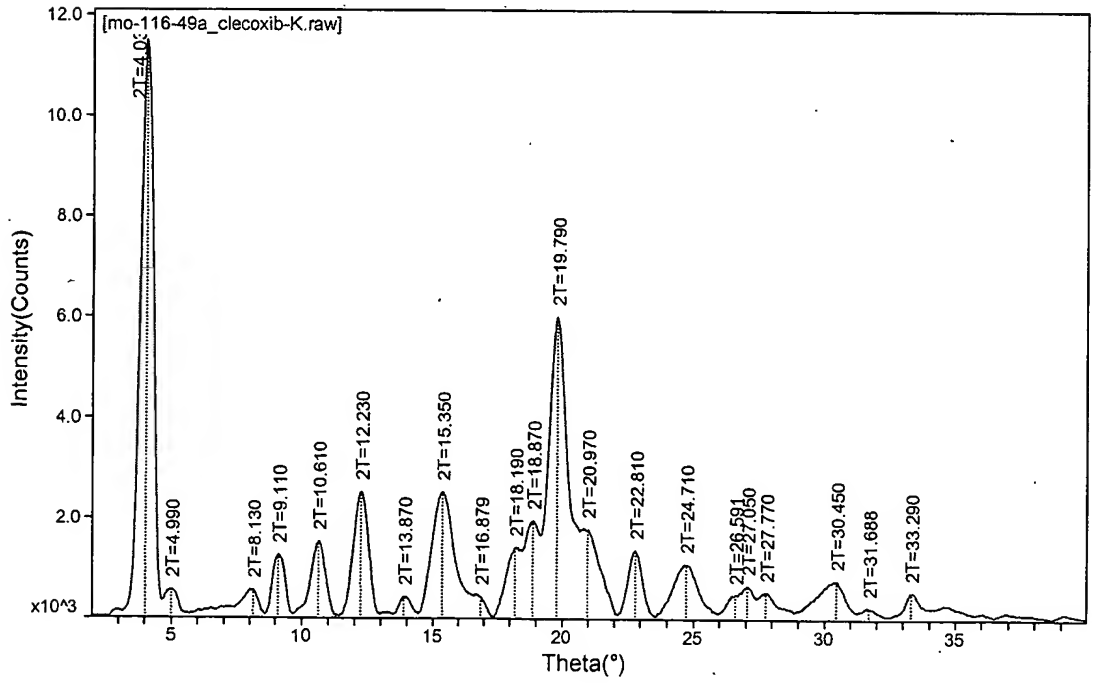


FIGURE 21

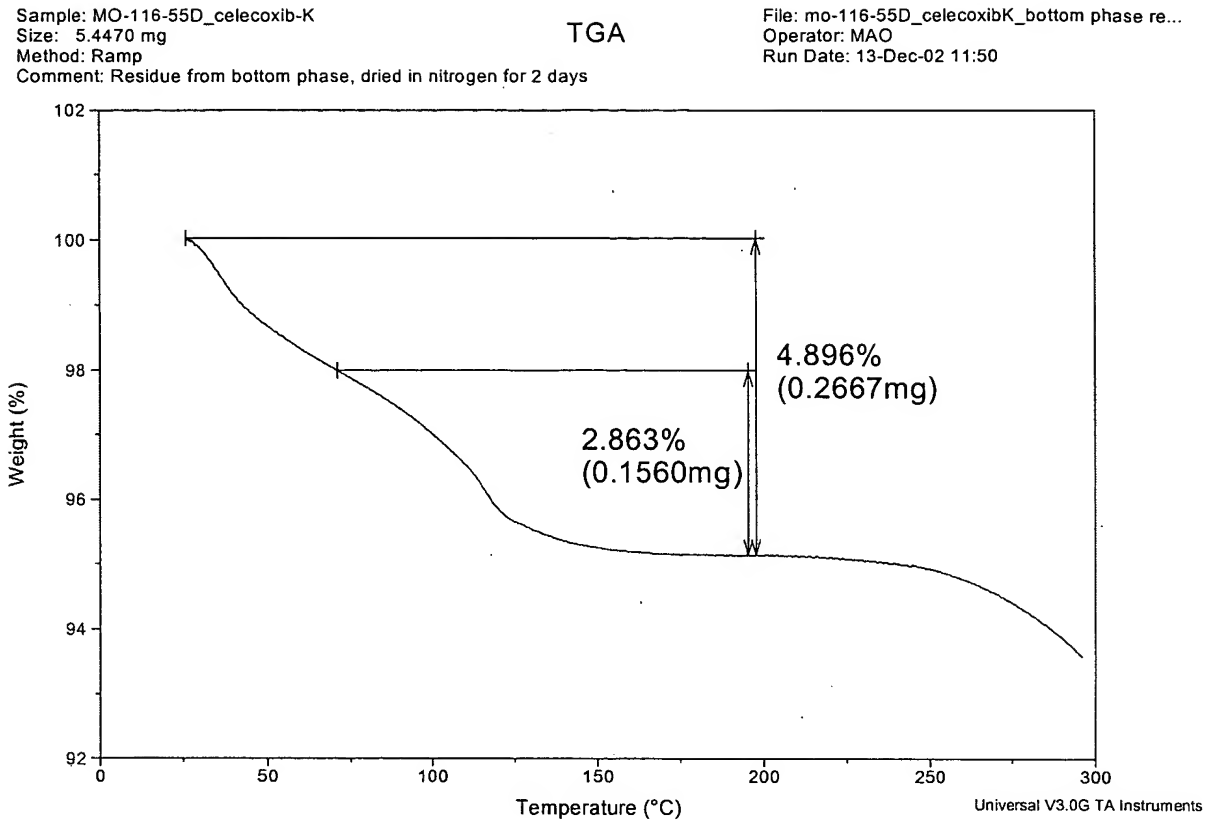

Sample: MO-116-55D_celecoxib-K
Size: 5.4470 mg
Method: Ramp
Comment: Residue from bottom phase, dried in nitrogen for 2 days
TGA
File: mo-116-55D_celecoxibK_bottom phase re...
Operator: MAO
Run Date: 13-Dec-02 11:50
4.896%
(0.2667mg)
2.863%
(0.1560mg)
Weight (%)
Temperature (°C)
Universal V3.0G TA Instruments

FIGURE 22

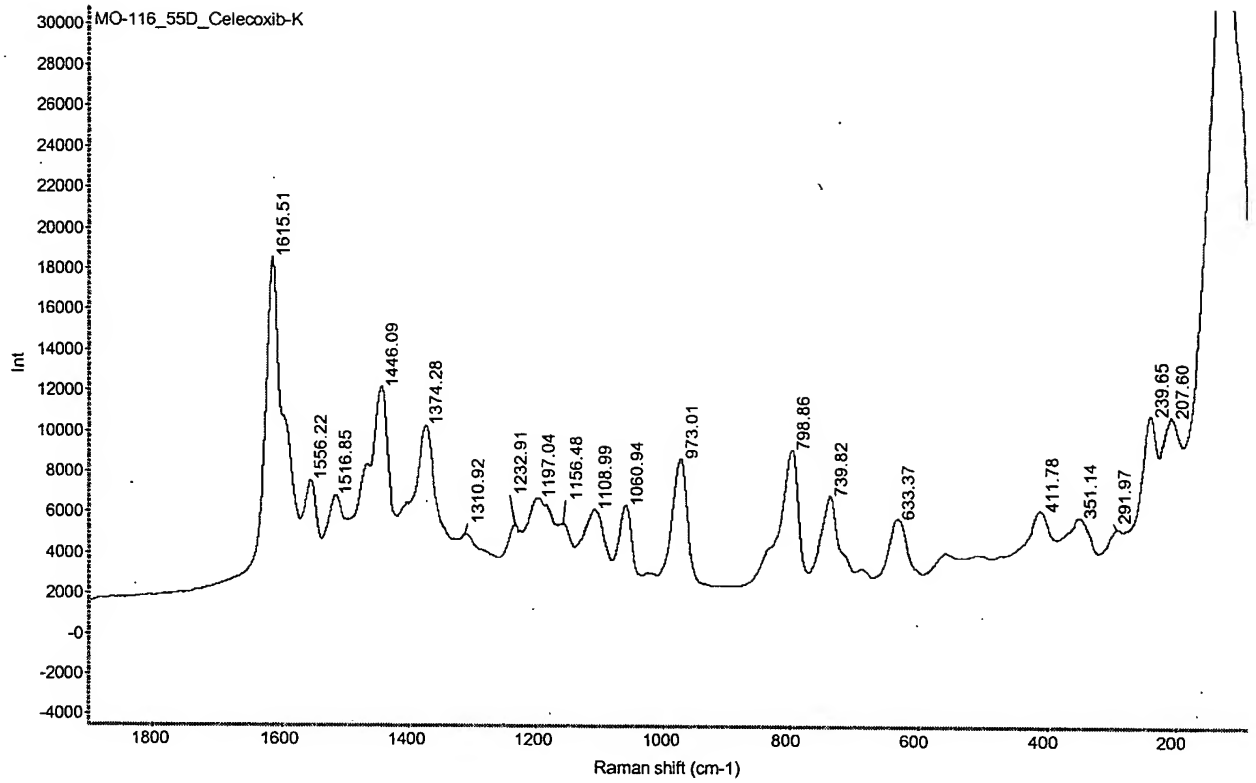


FIGURE 23

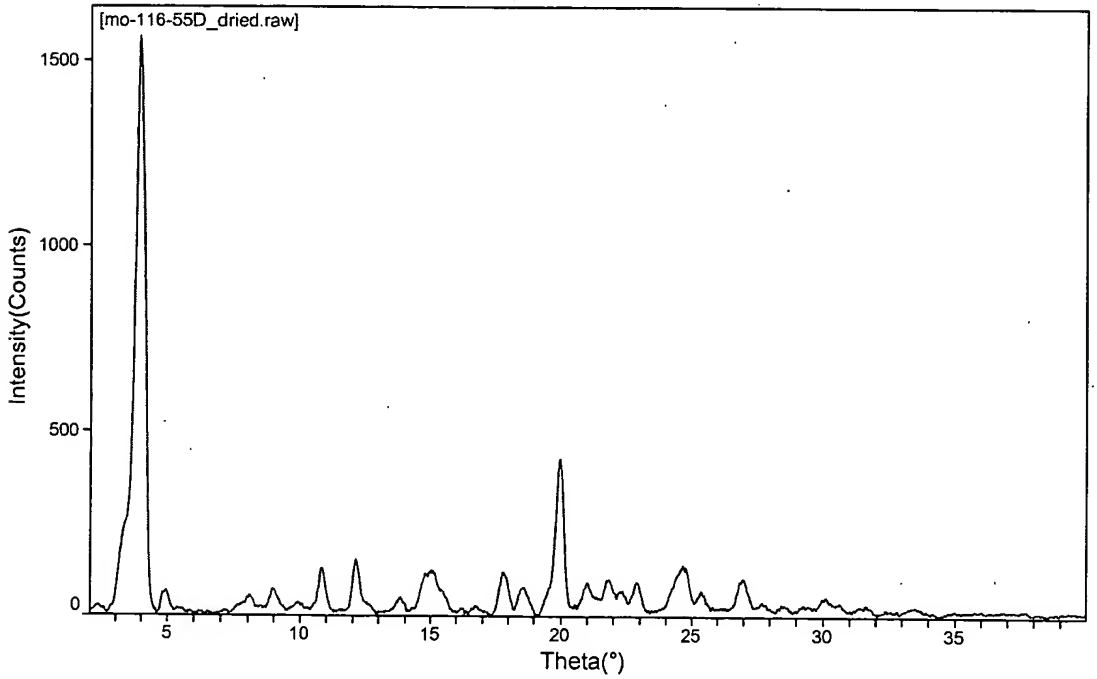


FIGURE 24

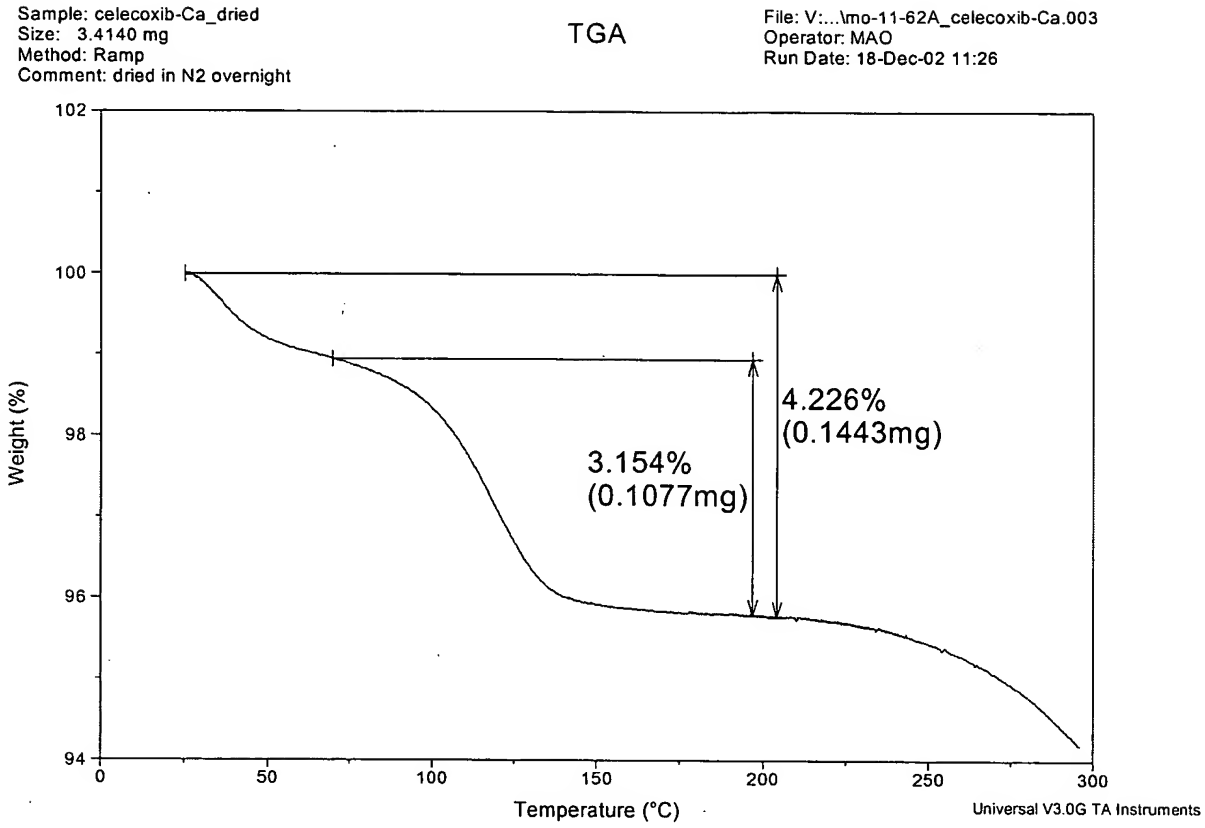

Sample: celecoxib-Ca_dried
Size: 3.4140 mg
Method: Ramp
Comment: dried in N2 overnight
TGA
File: V:...\mo-11-62A_celecoxib-Ca.003
Operator: MAO
Run Date: 18-Dec-02 11:26
102
100
98
96
94
Weight (%)
4.226%
(0.1443mg)
3.154%
(0.1077mg)
0
50
100
150
200
250
300
Temperature (°C)
Universal V3.0G TA Instruments

FIGURE 25

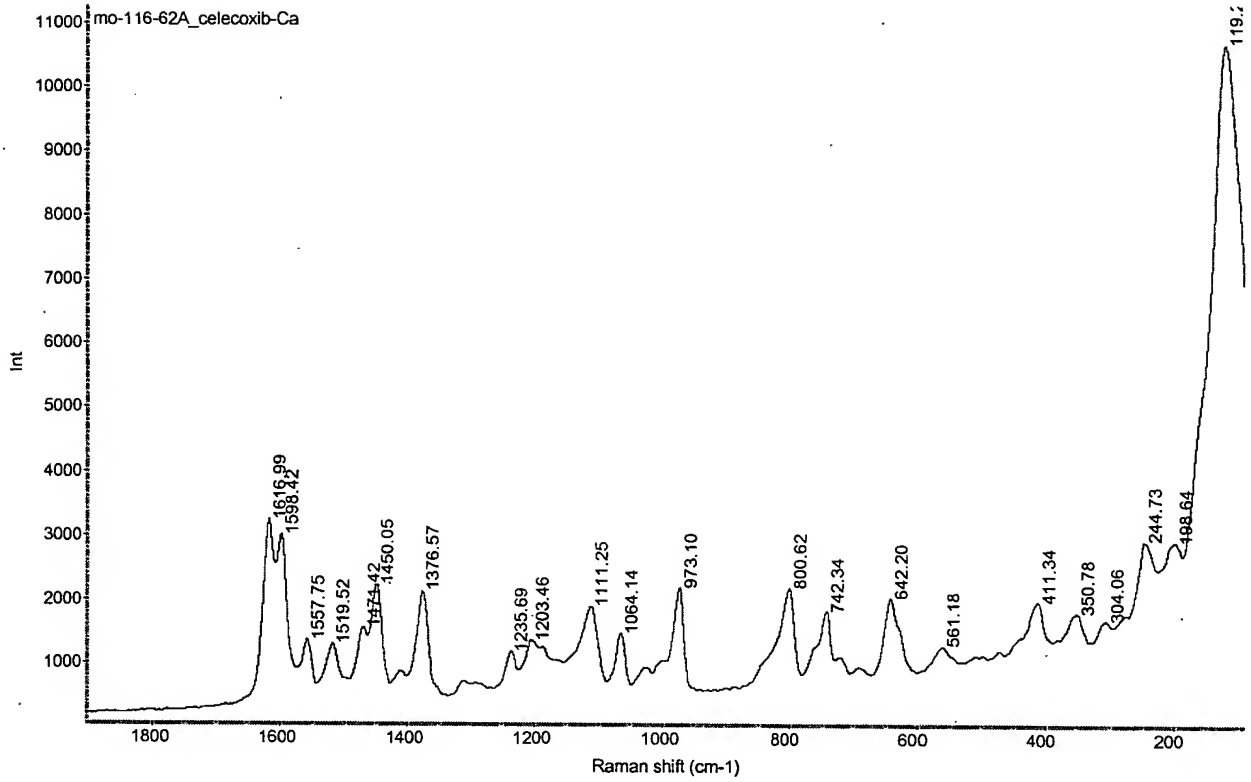

mo-116-62A_celecoxib-Ca
Int
Raman shift (cm-1)
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
1800
1600
1400
1200
1000
800
600
400
200
1616.99
1598.42
1557.75
1519.52
1450.05
1376.57
1235.69
1203.46
1111.25
1064.14
973.10
800.62
742.34
642.20
561.18
411.34
350.78
304.06
244.73

FIGURE 26

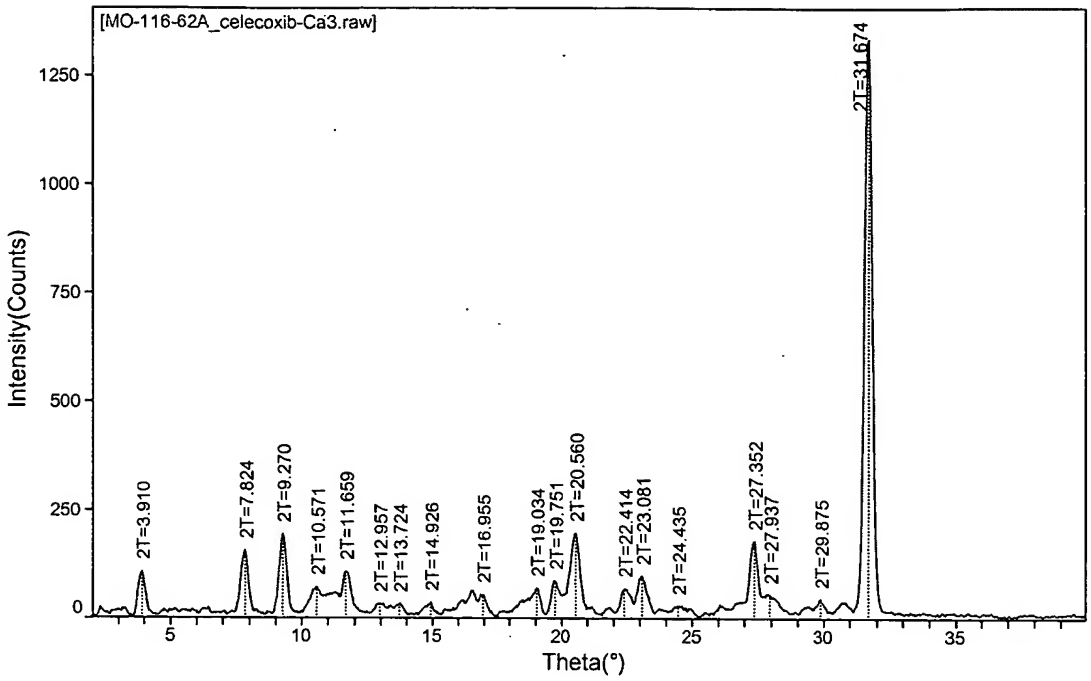


FIGURE 27

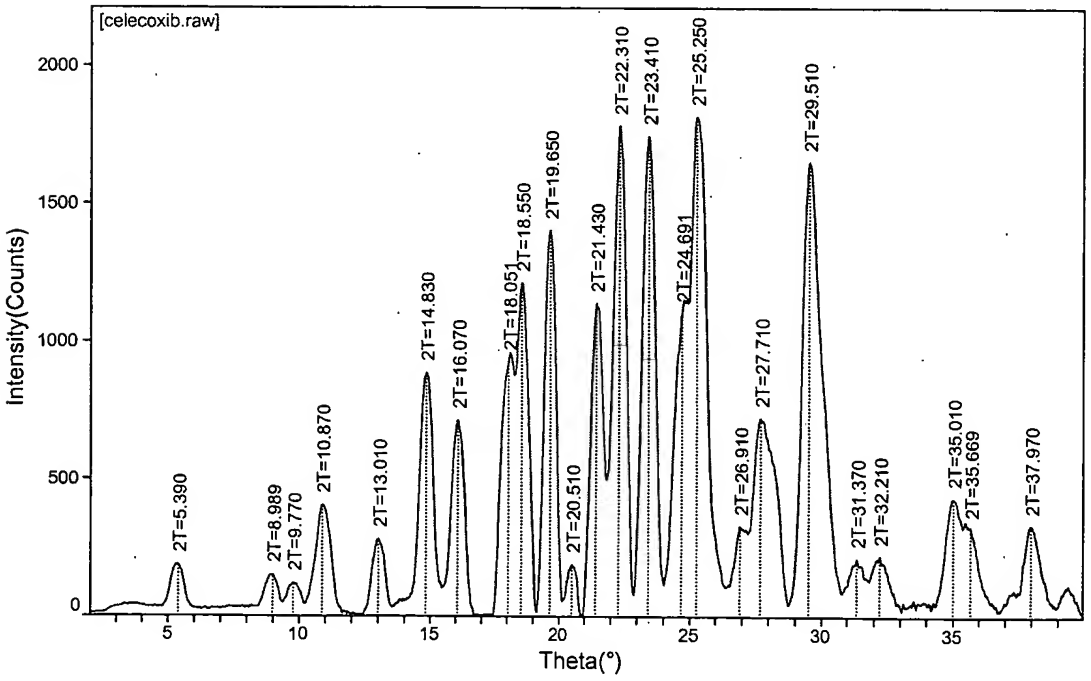


FIGURE 28

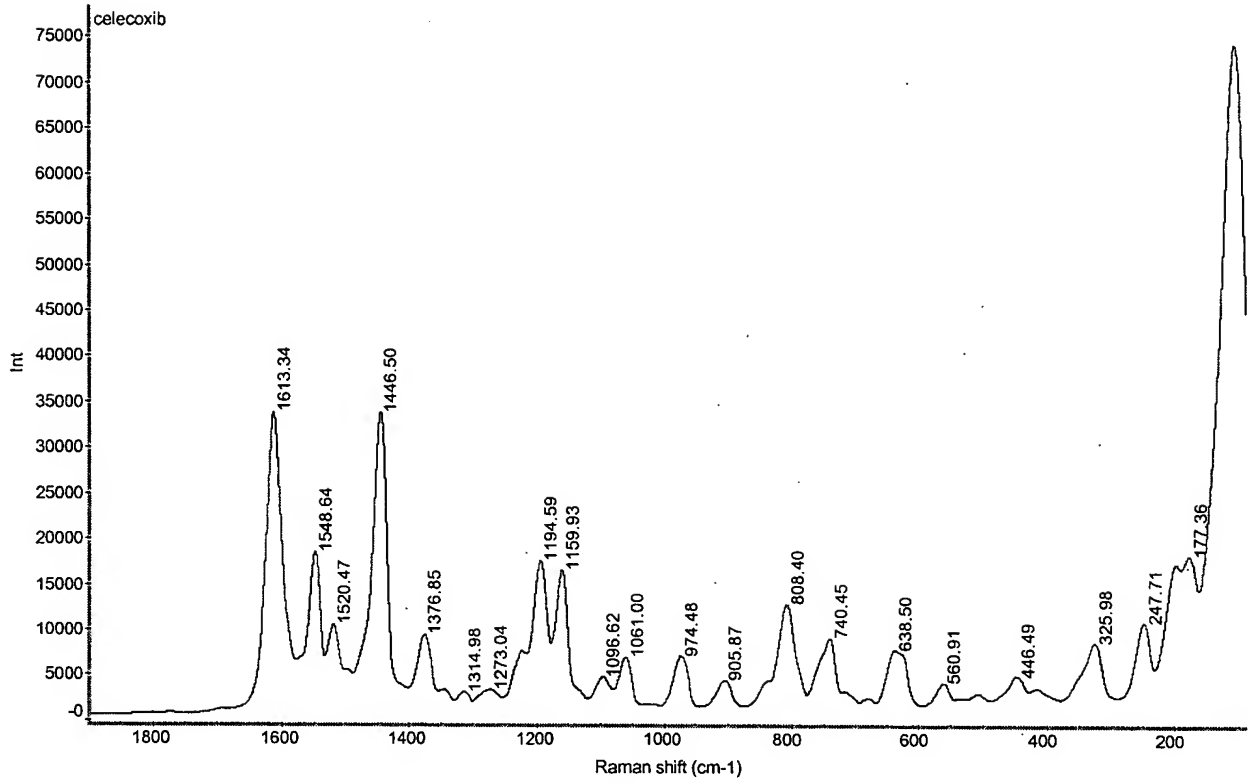

celecoxib
Int
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
-0
1613.34
1548.64
1520.47
1446.50
1376.85
1314.98
1273.04
1194.59
1159.93
1096.62
1061.00
974.48
905.87
808.40
740.45
638.50
560.91
446.49
325.98
247.71
177.36
1800
1600
1400
1200
1000
800
600
400
200
Raman shift (cm-1)

FIGURE 29

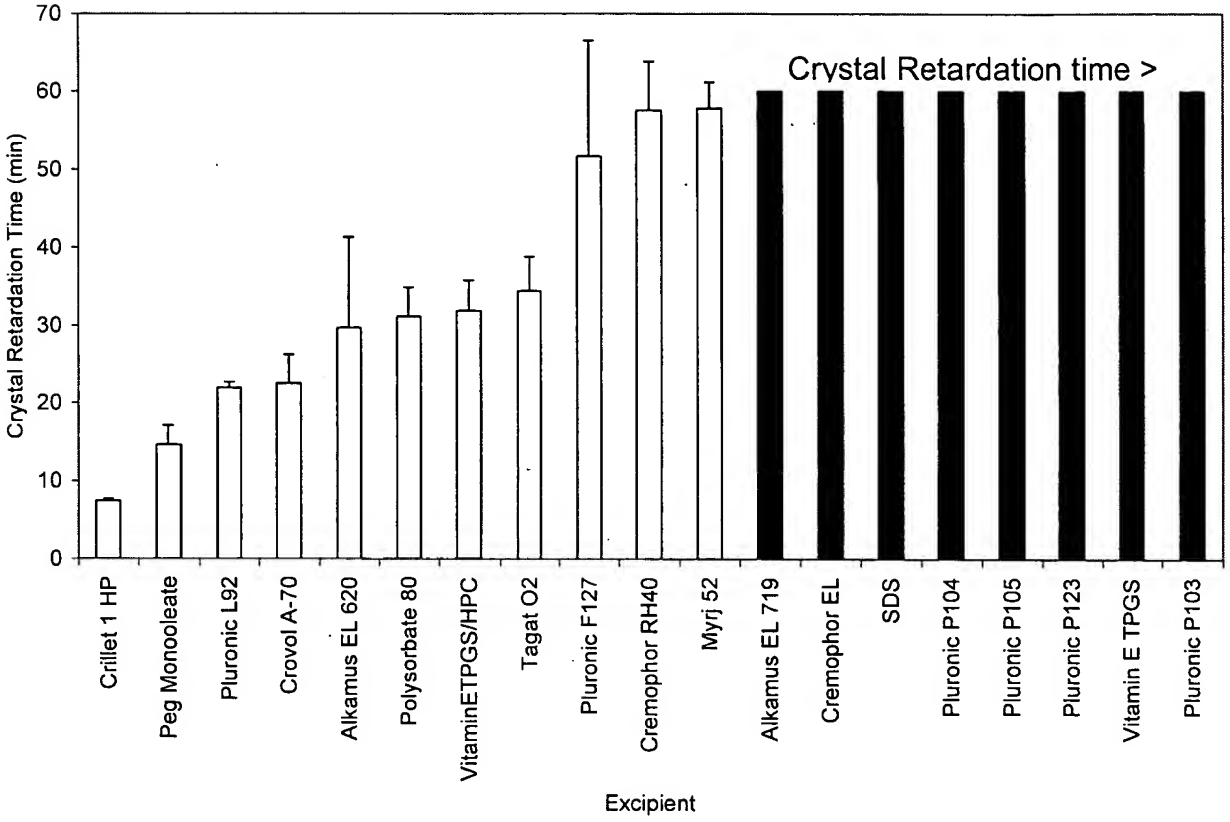

Crystal Retardation time >
Crystal Retardation Time (min)
70
60
50
40
30
20
10
0
Crillet 1 HP
Peg Monooleate
Pluronic L92
Crovol A-70
Alkamus EL 620
Polysorbate 80
VitaminETPGS/HPC
Tagat O2
Pluronic F127
Cremophor RH40
Myrj 52
Alkamus EL 719
Cremophor EL
SDS
Pluronic P104
Pluronic P105
Pluronic P123
Vitamin E TPGS
Pluronic P103
Excipient

FIGURE 30

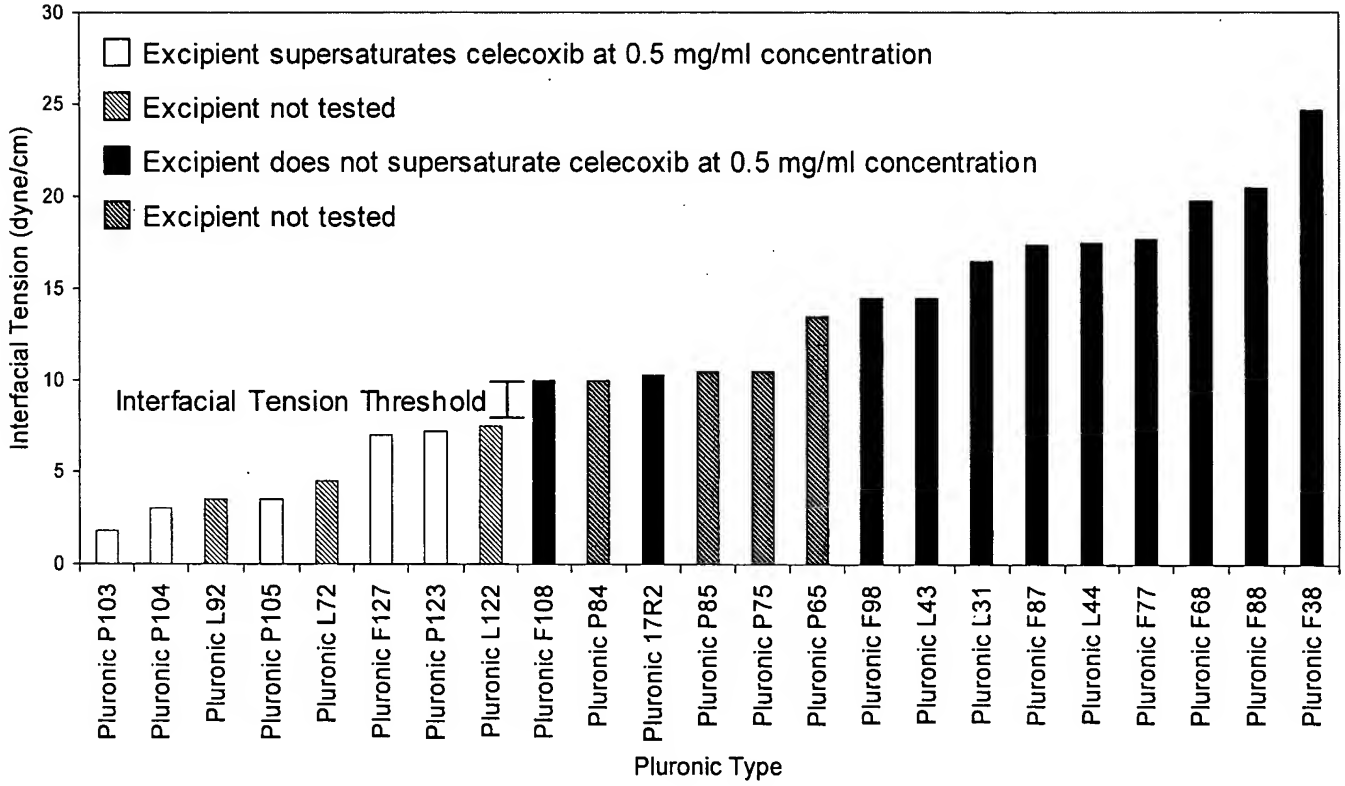

Excipient supersaturates celecoxib at 0.5 mg/ml concentration
Excipient not tested
Excipient does not supersaturate celecoxib at 0.5 mg/ml concentration
Excipient not tested
Interfacial Tension Threshold
Interfacial Tension (dyne/cm)
30
25
20
15
10
5
0
Pluronic P103
Pluronic P104
Pluronic L92
Pluronic P105
Pluronic L72
Pluronic F127
Pluronic P123
Pluronic L122
Pluronic F108
Pluronic P84
Pluronic 17R2
Pluronic P85
Pluronic P75
Pluronic P65
Pluronic F98
Pluronic L43
Pluronic L31
Pluronic F87
Pluronic L44
Pluronic F77
Pluronic F68
Pluronic F88
Pluronic F38
Pluronic Type

Figure 31

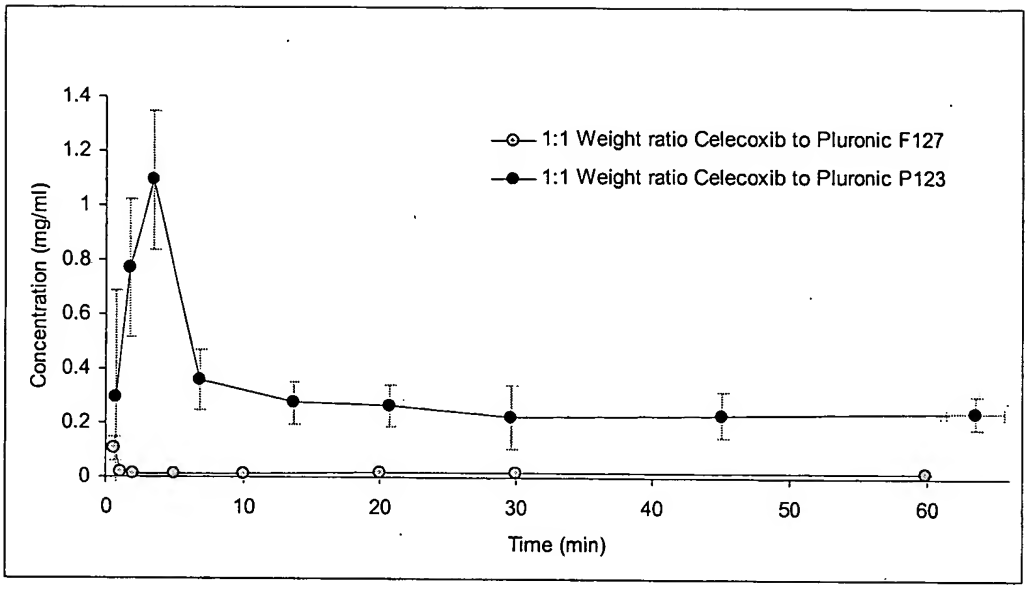

1.4
1.2
1
0.8
0.6
0.4
0.2
0
Concentration (mg/ml)
0
10
20
30
40
50
60
Time (min)
1:1 Weight ratio Celecoxib to Pluronic F127
1:1 Weight ratio Celecoxib to Pluronic P123

Figure 32

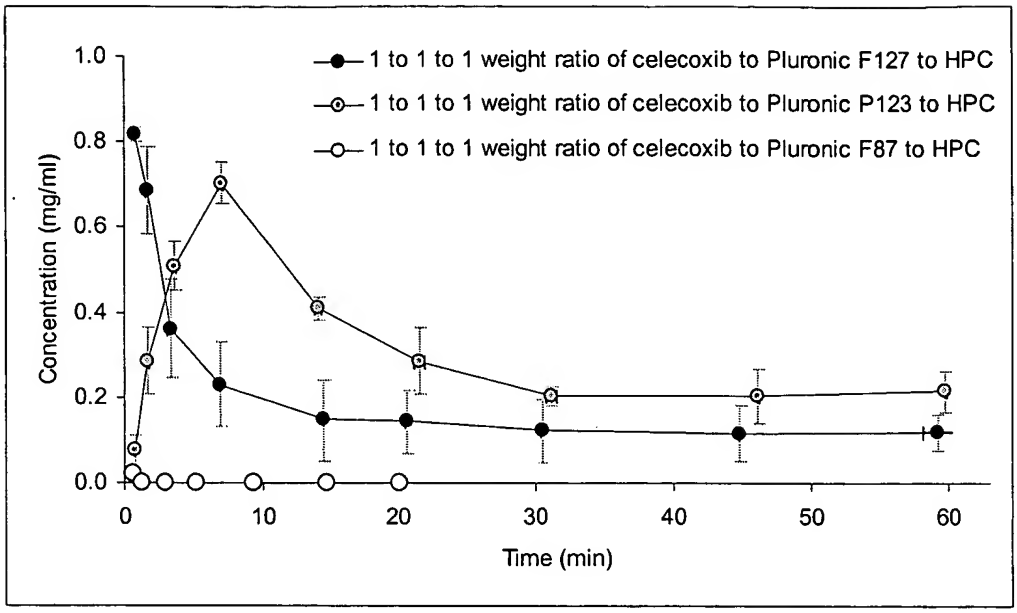

1 to 1 to 1 weight ratio of celecoxib to Pluronic F127 to HPC
1 to 1 to 1 weight ratio of celecoxib to Pluronic P123 to HPC
1 to 1 to 1 weight ratio of celecoxib to Pluronic F87 to HPC
Concentration (mg/ml)
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
60
Time (min)

Figure 33

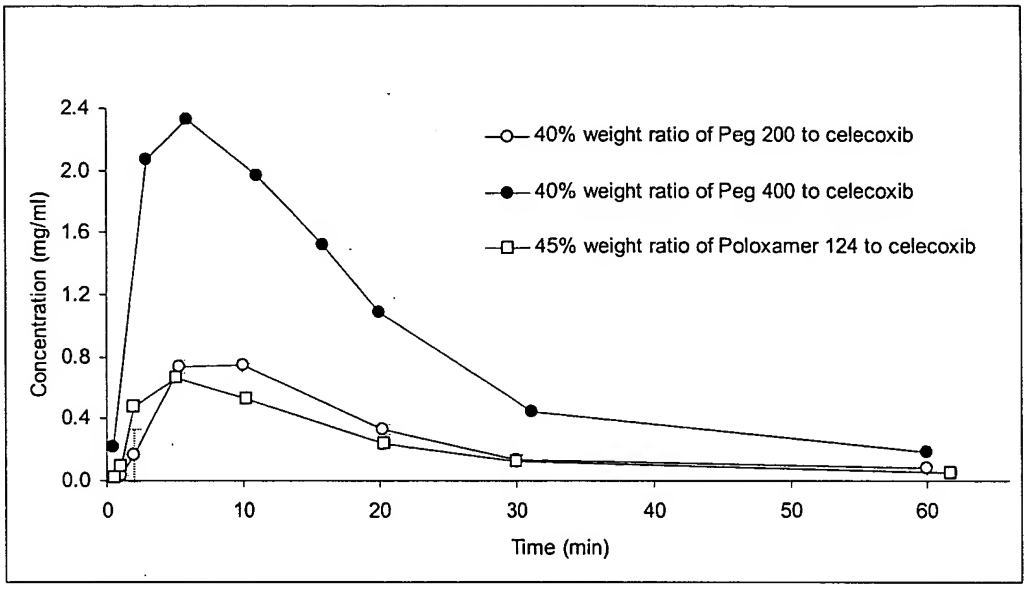

Concentration (mg/ml)
2.4
2.0
1.6
1.2
0.8
0.4
0.0
0
10
20
30
40
50
60
Time (min)
40% weight ratio of Peg 200 to celecoxib
40% weight ratio of Peg 400 to celecoxib
45% weight ratio of Poloxamer 124 to celecoxib

Figure 34

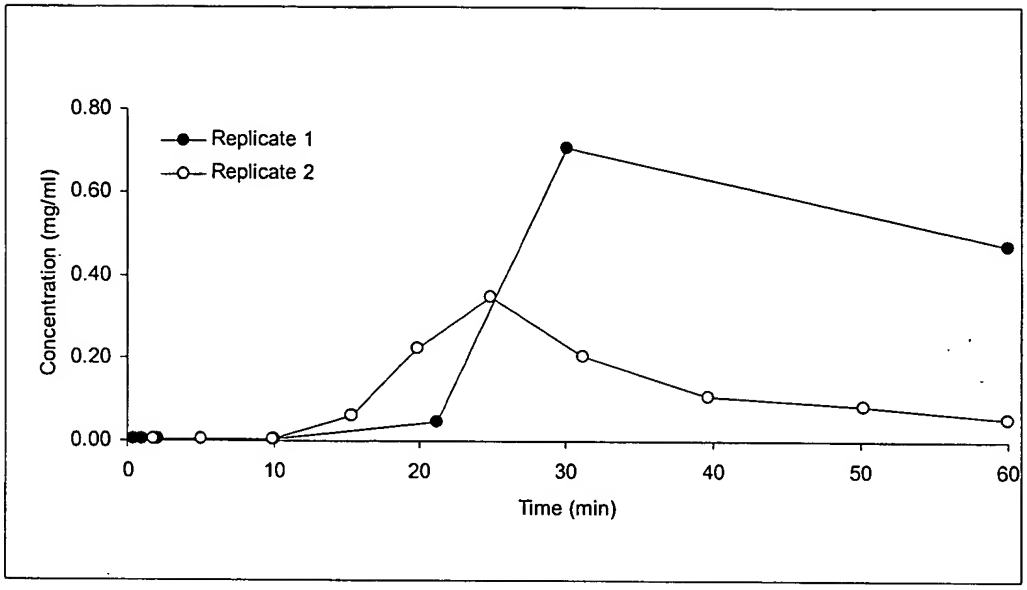

0.80
0.60
0.40
0.20
0.00
Concentration (mg/ml)
Replicate 1
Replicate 2
0
10
20
30
40
50
60
Time (min)

Figure 35

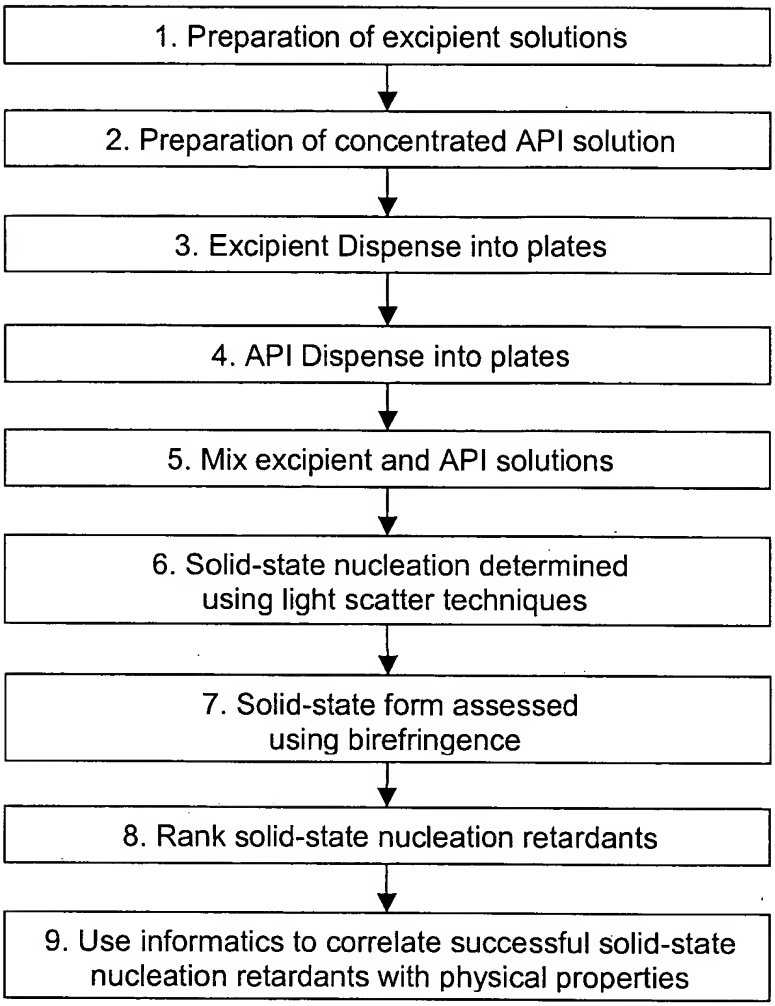

1. Preparation of excipient solutions
2. Preparation of concentrated API solution
3. Excipient Dispense into plates
4. API Dispense into plates
5. Mix excipient and API solutions
6. Solid-state nucleation determined using light scatter techniques
7. Solid-state form assessed using birefringence
8. Rank solid-state nucleation retardants
9. Use informatics to correlate successful solid-state nucleation retardants with physical properties

Figure 36

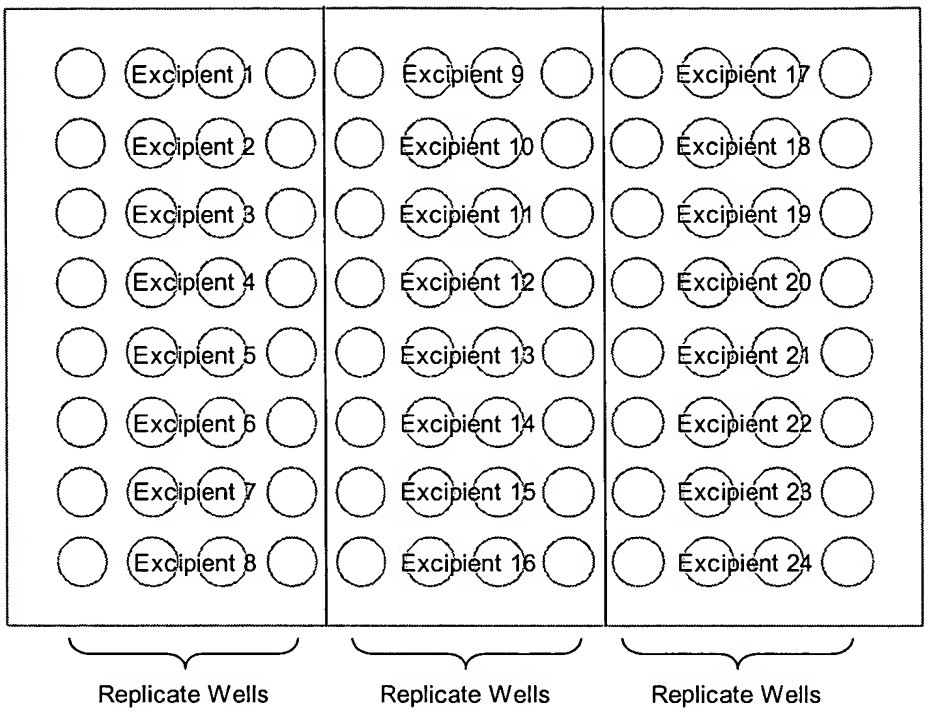

Excipient 1
Excipient 2
Excipient 3
Excipient 4
Excipient 5
Excipient 6
Excipient 7
Excipient 8
Excipient 9
Excipient 10
Excipient 11
Excipient 12
Excipient 13
Excipient 14
Excipient 15
Excipient 16
Excipient 17
Excipient 18
Excipient 19
Excipient 20
Excipient 21
Excipient 22
Excipient 23
Excipient 24
Replicate Wells
Replicate Wells
Replicate Wells

Figure 37

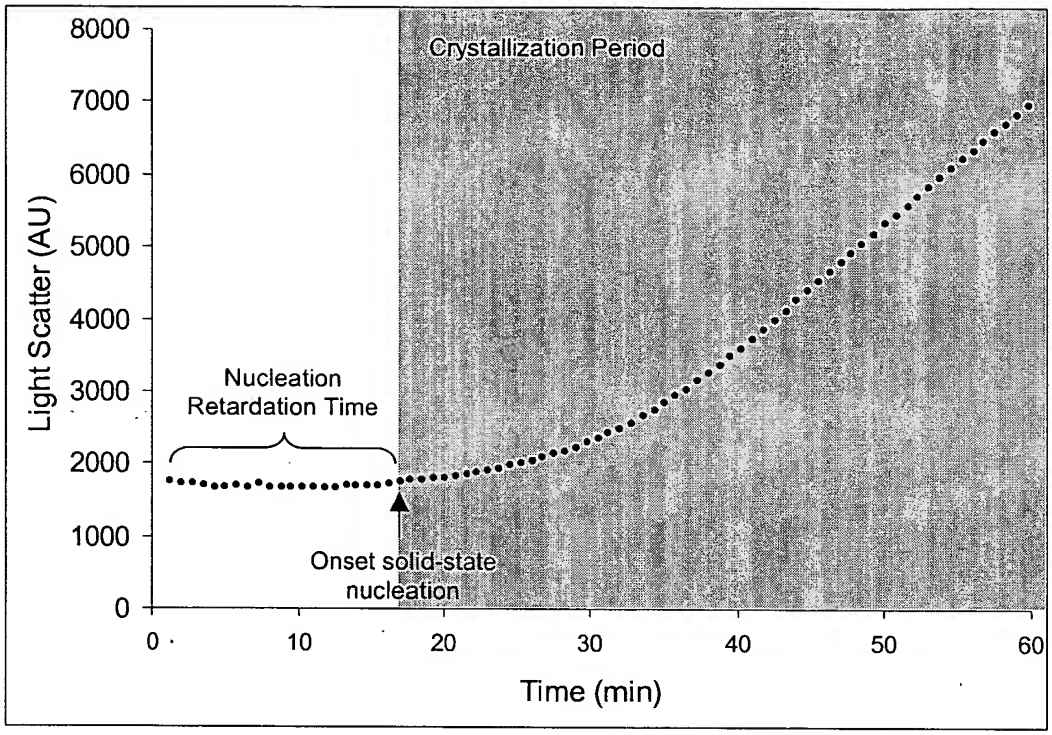

Crystallization Period
Nucleation
Retardation Time
Onset solid-state
nucleation
Light Scatter (AU)
Time (min)
8000
7000
6000
5000
4000
3000
2000
1000
0
0
10
20
30
40
50
60

Figure 38

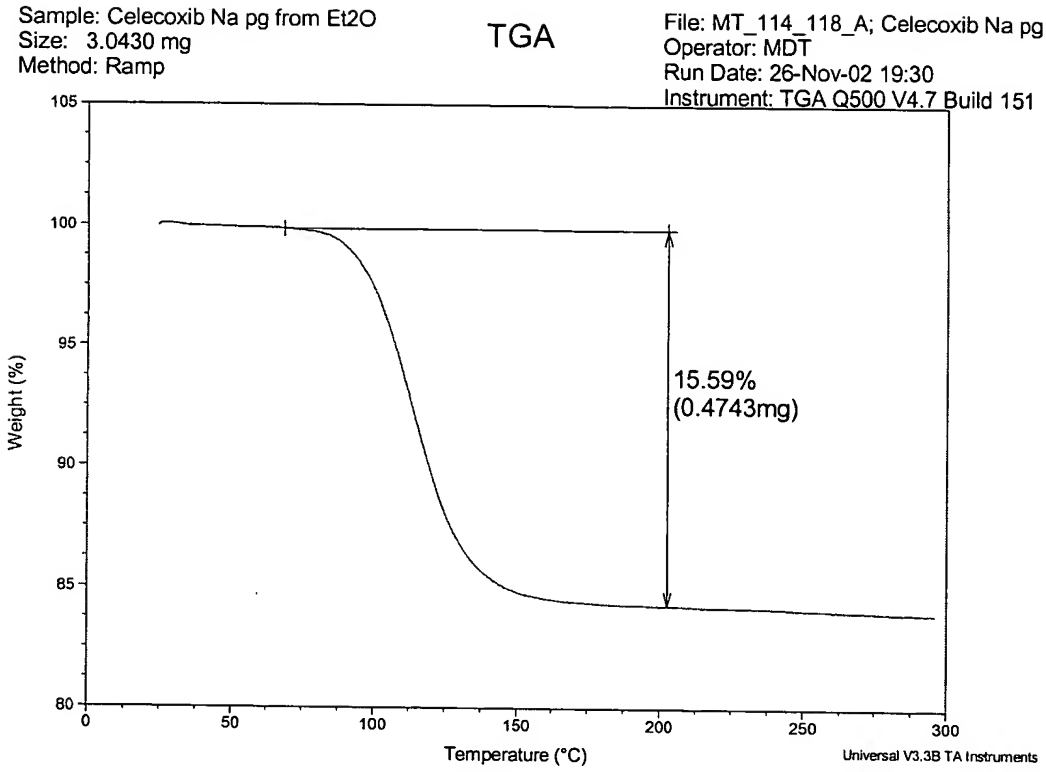

Sample: Celecoxib Na pg from Et2O
Size: 3.0430 mg
Method: Ramp
TGA
File: MT_114_118_A; Celecoxib Na pg
Operator: MDT
Run Date: 26-Nov-02 19:30
Instrument: TGA Q500 V4.7 Build 151
105
100
95
90
85
80
Weight (%)
15.59%
(0.4743mg)
0
50
100
150
200
250
300
Temperature (°C)
Universal V3.3B TA Instruments

FIGURE 39

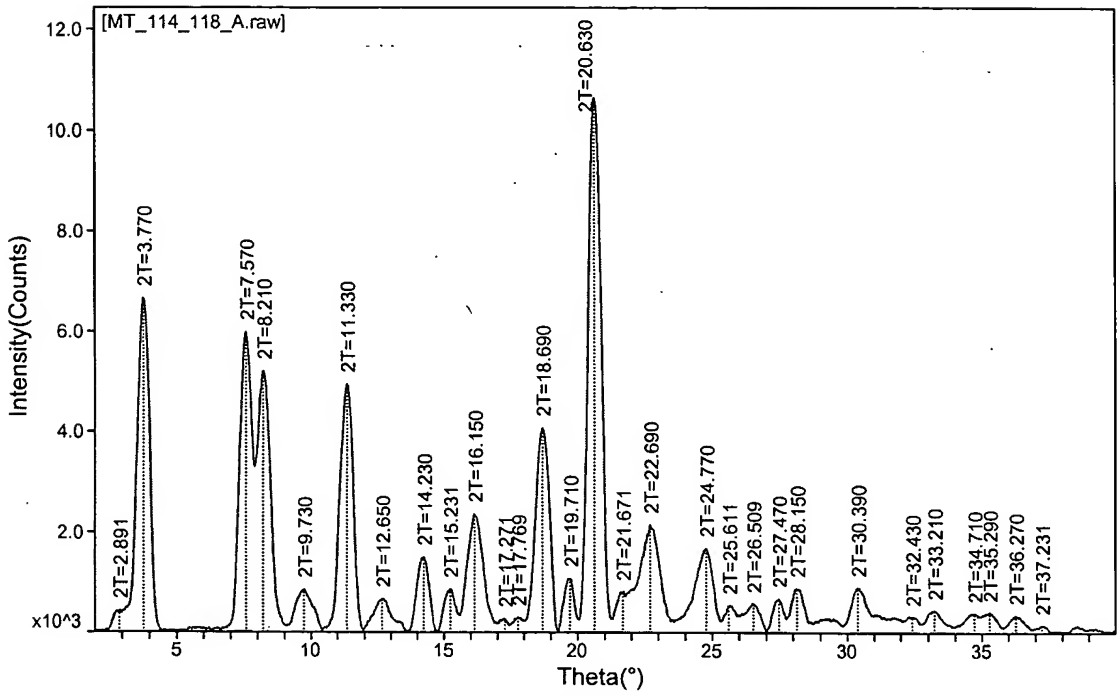


FIGURE 40

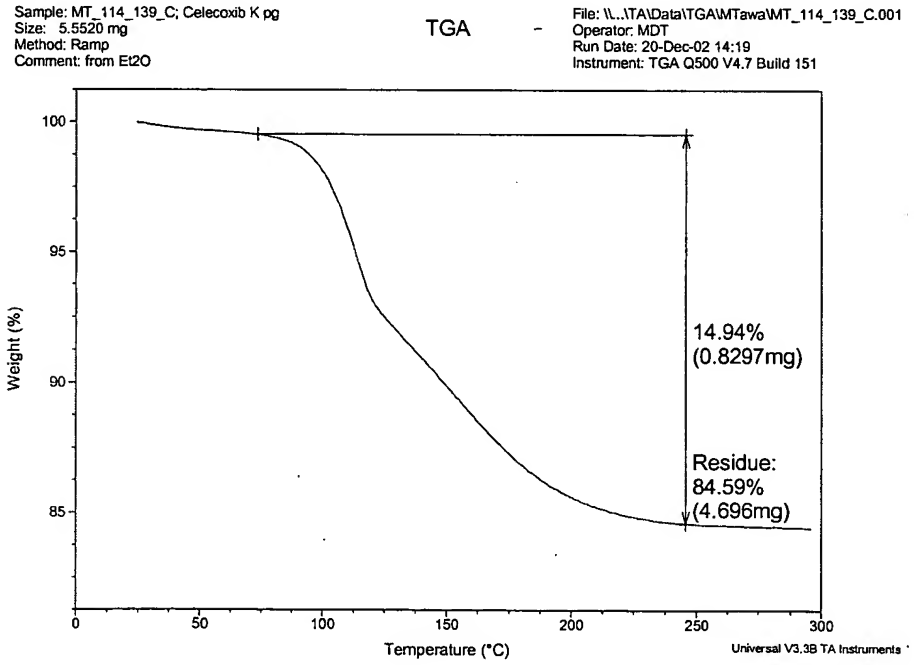


FIGURE 41

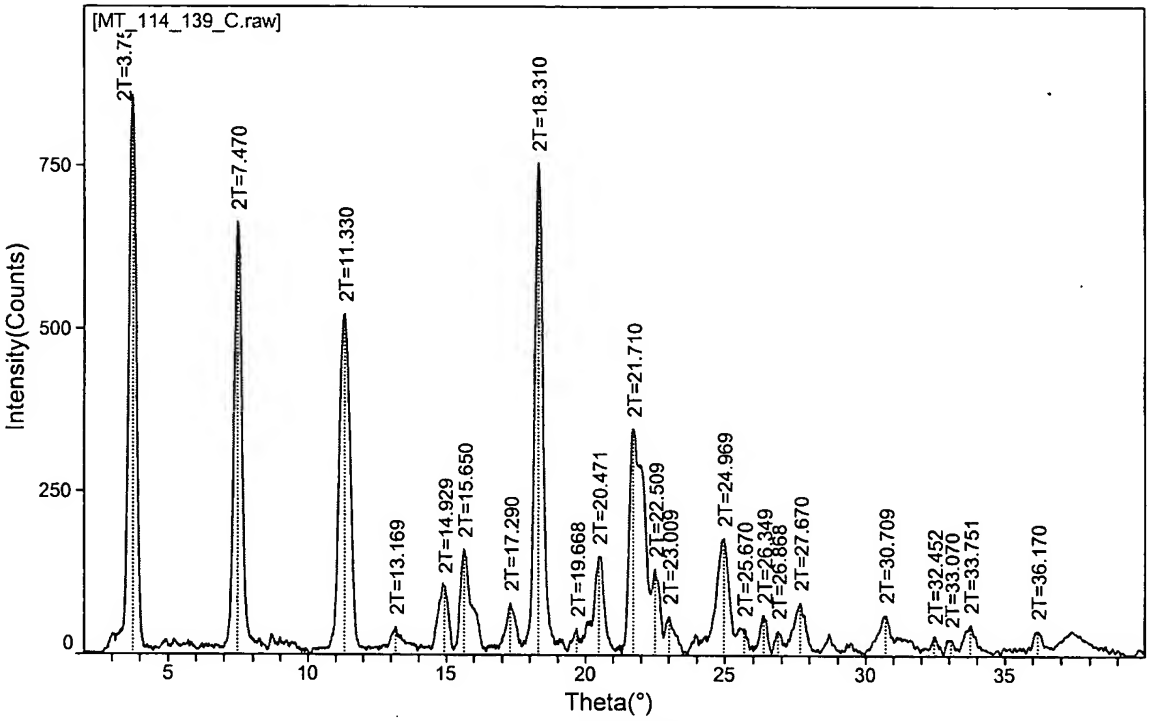

[MT_114_139_C.raw]
Intensity(Counts)
750
500
250
0
5
10
15
20
25
30
35
Theta(°)
2T=3.75
2T=7.470
2T=11.330
2T=13.169
2T=14.929
2T=15.650
2T=17.290
2T=18.310
2T=19.668
2T=20.471
2T=21.710
2T=22.509
2T=23.009
2T=24.969
2T=25.670
2T=26.349
2T=26.868
2T=27.670
2T=30.709
2T=32.452
2T=33.070
2T=33.751
2T=36.170

FIGURE 42

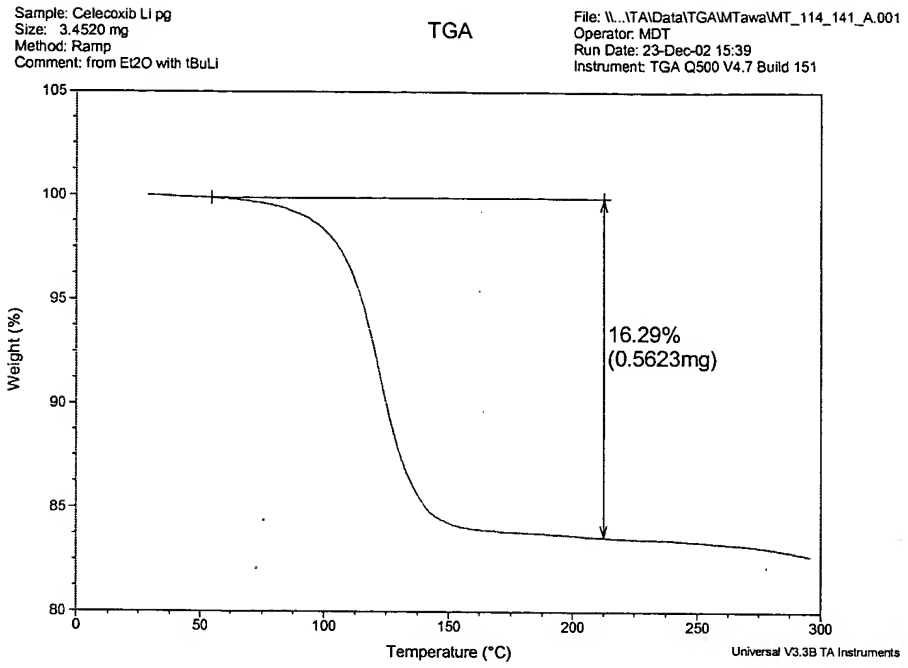

Sample: Celecoxib Li pg
Size: 3.4520 mg
Method: Ramp
Comment: from Et2O with tBuLi
TGA
File: \\...\TA\Data\TGA\MTawa\MT_114_141_A.001
Operator: MDT
Run Date: 23-Dec-02 15:39
Instrument: TGA Q500 V4.7 Build 151
Weight (%)
105
100
95
90
85
80
16.29%
(0.5623mg)
0
50
100
150
200
250
300
Temperature (°C)
Universal V3.3B TA Instruments

FIGURE 43

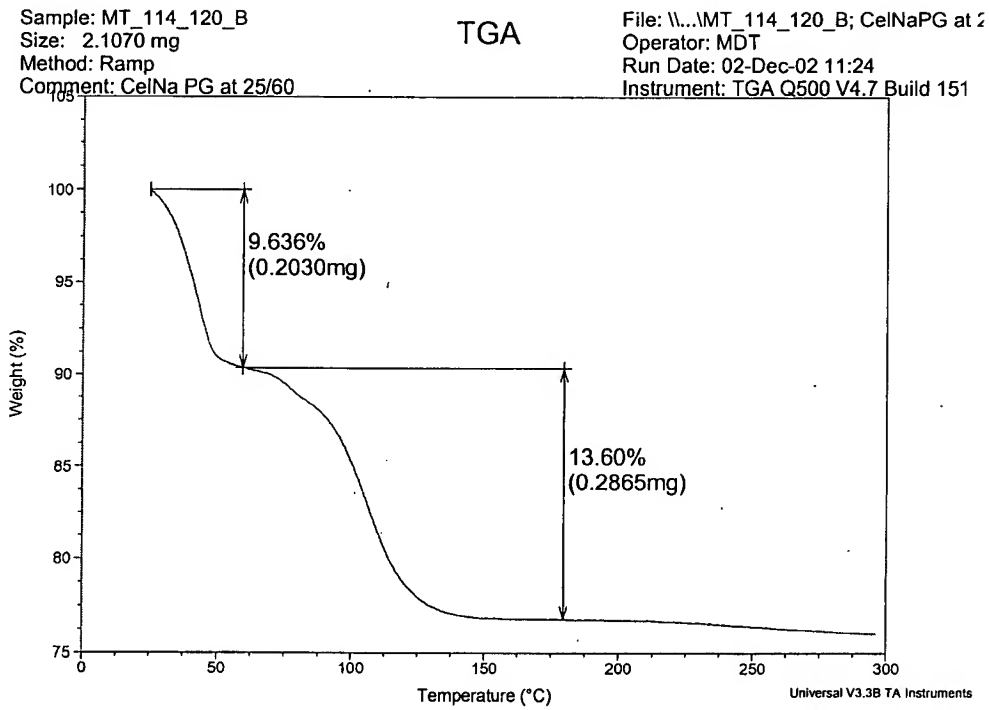

Sample: MT_114_120_B
Size: 2.1070 mg
Method: Ramp
Comment: CelNa PG at 25/60
TGA
File: \\...\MT_114_120_B; CelNaPG at 2
Operator: MDT
Run Date: 02-Dec-02 11:24
Instrument: TGA Q500 V4.7 Build 151
9.636%
(0.2030mg)
13.60%
(0.2865mg)
Weight (%)
Temperature (°C)
Universal V3.3B TA Instruments

FIGURE 44

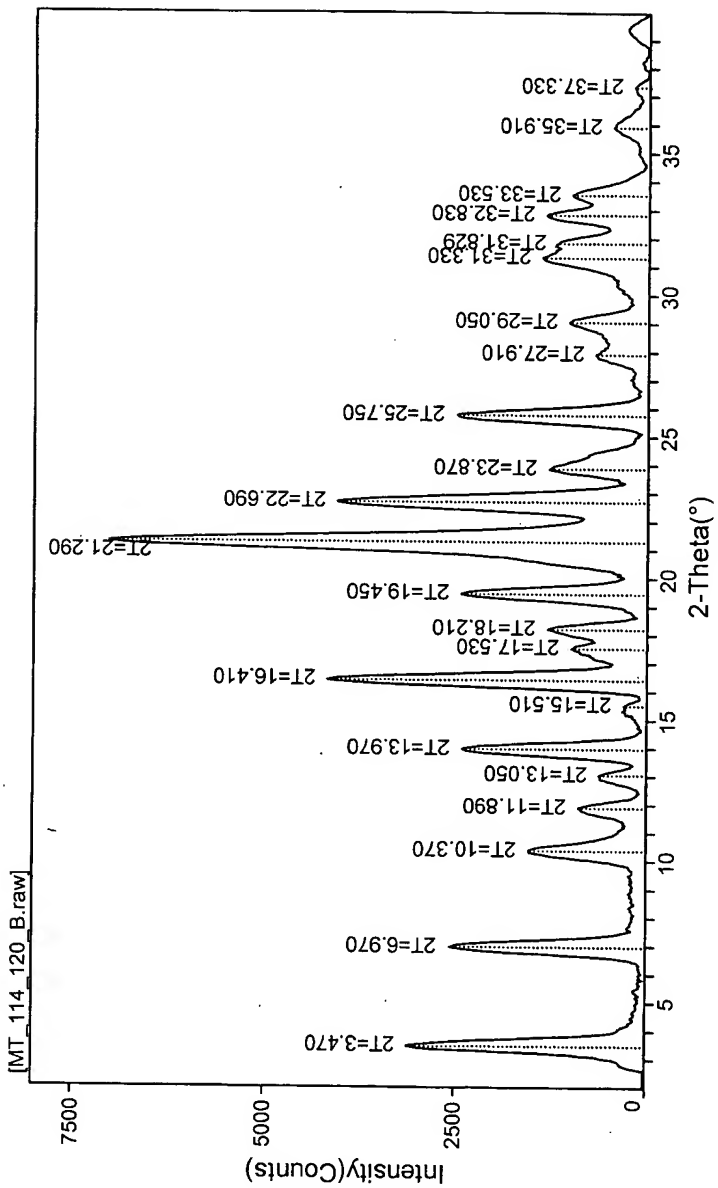

[MT_114_120_B.raw]
Intensity(Counts)
7500
5000
2500
0
2-Theta(°)
5
10
15
20
25
30
35
2T=3.470
2T=6.970
2T=10.370
2T=11.890
2T=13.050
2T=13.970
2T=15.510
2T=16.410
2T=17.530
2T=18.210
2T=19.450
2T=21.290
2T=22.690
2T=23.870
2T=25.750
2T=27.910
2T=29.050
2T=31.330
2T=31.829
2T=32.830
2T=33.530
2T=35.910
2T=37.330

FIGURE 45

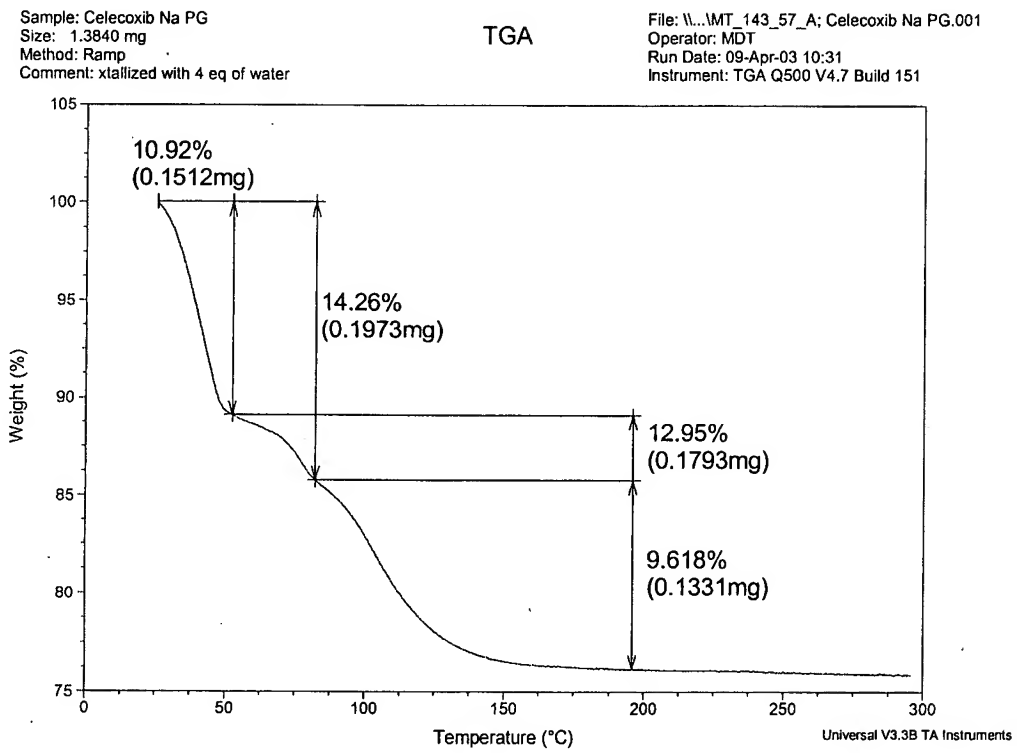

Sample: Celecoxib Na PG
Size: 1.3840 mg
Method: Ramp
Comment: xtallized with 4 eq of water
TGA
File: \\...\MT_143_57_A; Celecoxib Na PG.001
Operator: MDT
Run Date: 09-Apr-03 10:31
Instrument: TGA Q500 V4.7 Build 151
10.92%
(0.1512mg)
14.26%
(0.1973mg)
12.95%
(0.1793mg)
9.618%
(0.1331mg)
Weight (%)
Temperature (°C)
Universal V3.3B TA Instruments

FIGURE 46

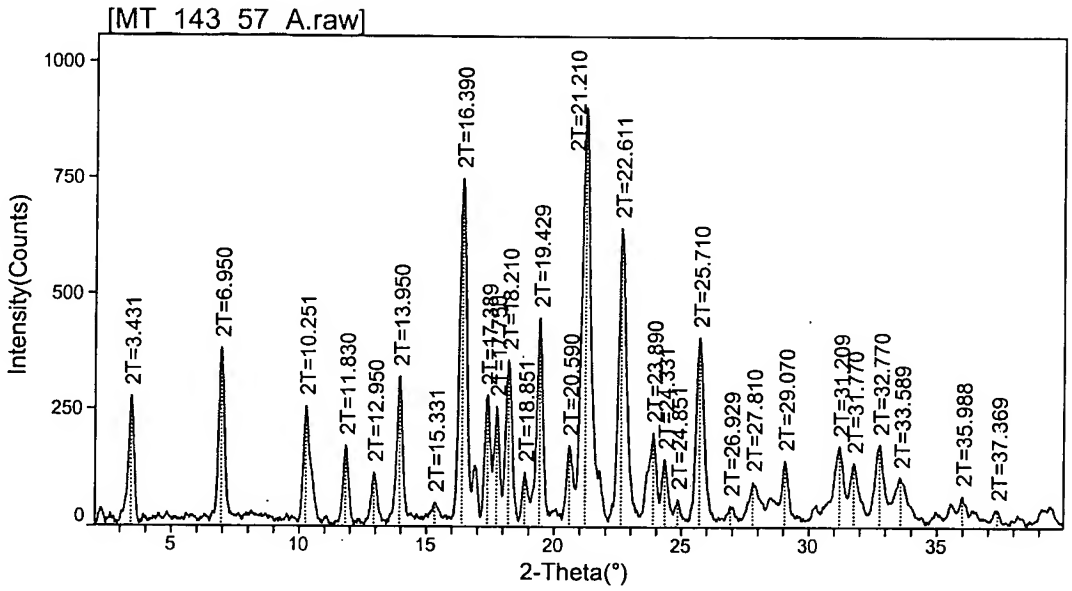

[MT_143_57_A.raw]
Intensity(Counts)
2-Theta(°)
2T=3.431
2T=6.950
2T=10.251
2T=11.830
2T=12.950
2T=13.950
2T=15.331
2T=16.390
2T=17.389
2T=18.210
2T=18.851
2T=19.429
2T=20.590
2T=21.210
2T=22.611
2T=23.890
2T=24.331
2T=24.851
2T=25.710
2T=26.929
2T=27.810
2T=29.070
2T=31.209
2T=31.770
2T=32.770
2T=33.589
2T=35.988
2T=37.369

FIGURE 47

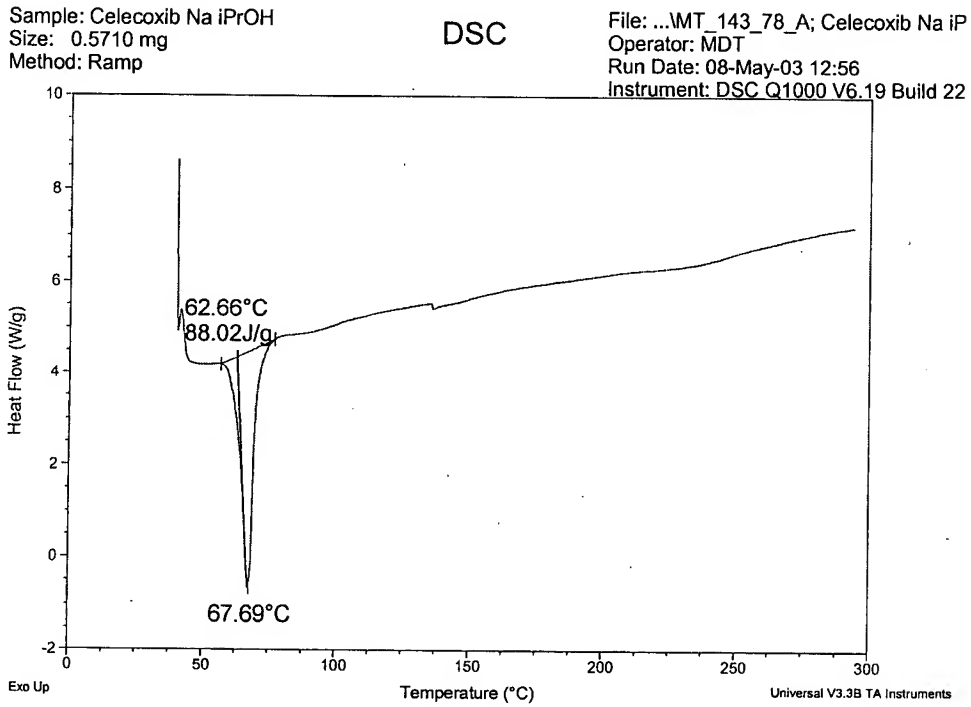

Sample: Celecoxib Na iPrOH
Size: 0.5710 mg
Method: Ramp
DSC
File: ...\MT_143_78_A; Celecoxib Na iP
Operator: MDT
Run Date: 08-May-03 12:56
Instrument: DSC Q1000 V6.19 Build 22
62.66°C
88.02J/g
67.69°C
Heat Flow (W/g)
Temperature (°C)
Exo Up
Universal V3.3B TA Instruments

FIGURE 48

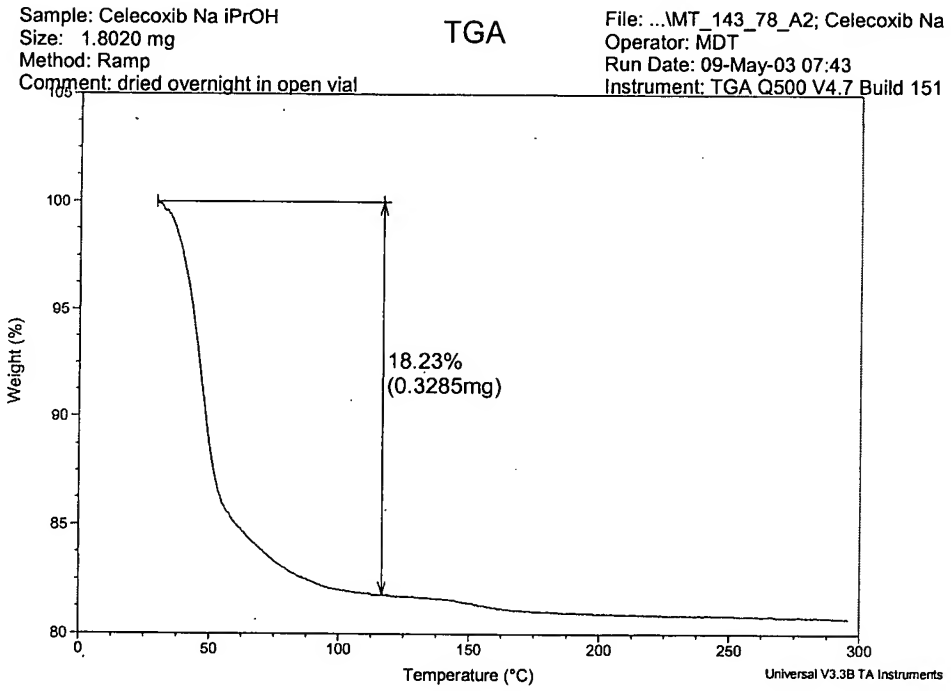

Sample: Celecoxib Na iPrOH
Size: 1.8020 mg
Method: Ramp
Comment: dried overnight in open vial
TGA
File: ...\MT_143_78_A2; Celecoxib Na i
Operator: MDT
Run Date: 09-May-03 07:43
Instrument: TGA Q500 V4.7 Build 151
Weight (%)
105
100
95
90
85
80
18.23%
(0.3285mg)
0
50
100
150
200
250
300
Temperature (°C)
Universal V3.3B TA Instruments

FIGURE 49

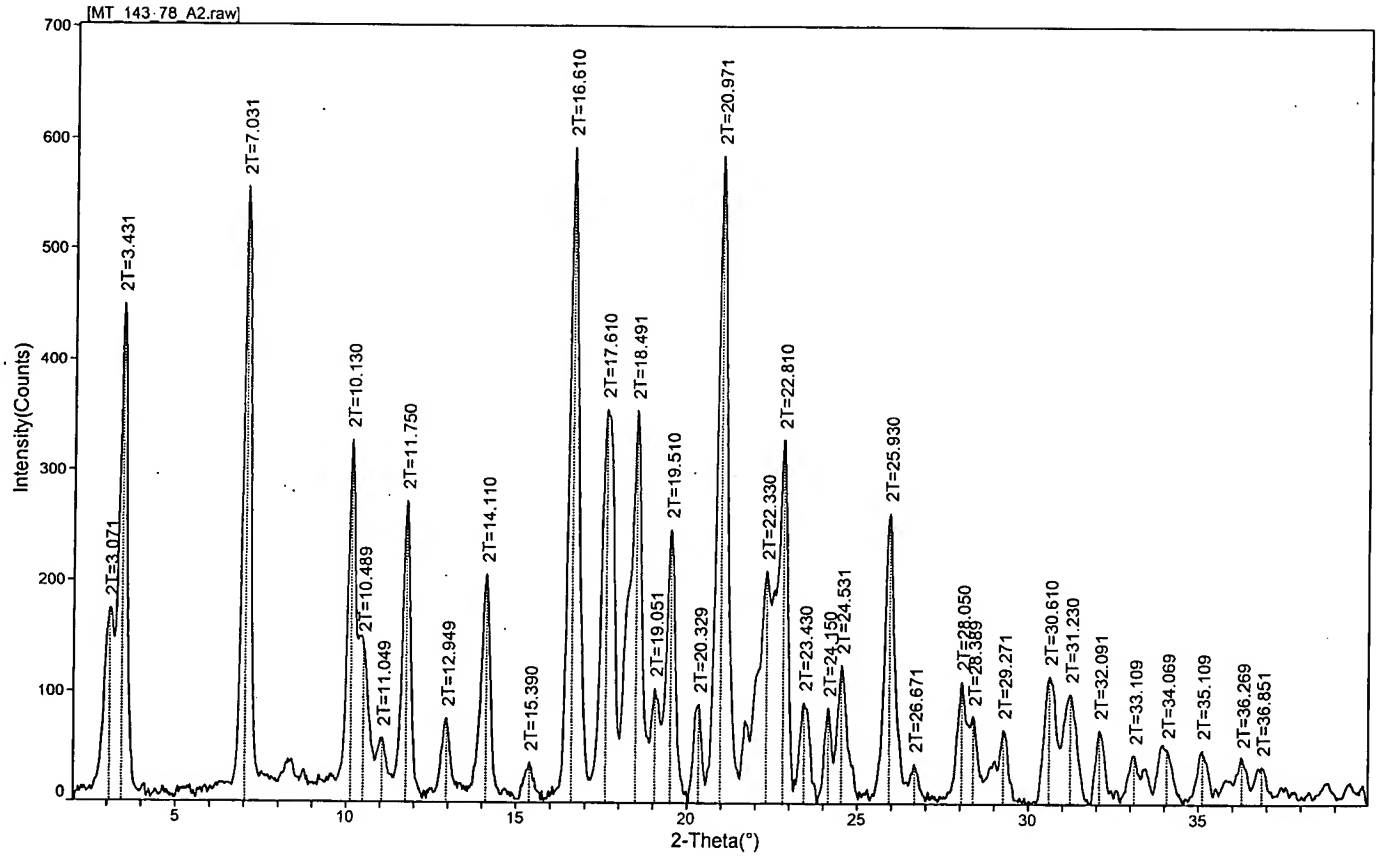

[MT_143_78_A2.raw]
Intensity(Counts)
2-Theta(°)
2T=3.071
2T=3.431
2T=7.031
2T=10.130
2T=10.489
2T=11.049
2T=11.750
2T=12.949
2T=14.110
2T=15.390
2T=16.610
2T=17.610
2T=18.491
2T=19.051
2T=19.510
2T=20.329
2T=20.971
2T=22.330
2T=22.810
2T=23.430
2T=24.150
2T=24.531
2T=25.930
2T=26.671
2T=28.050
2T=28.389
2T=29.271
2T=30.610
2T=31.230
2T=32.091
2T=33.109
2T=34.069
2T=35.109
2T=36.269
2T=36.851

FIGURE 50

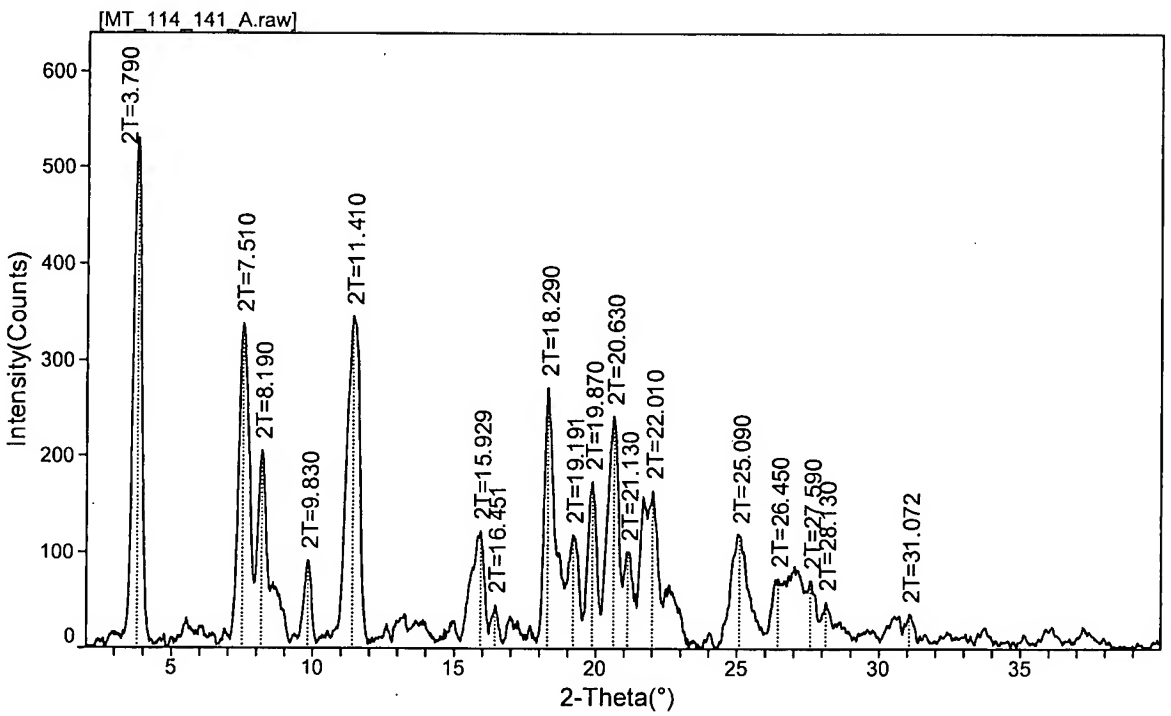

[MT_114_141_A.raw]
Intensity(Counts)
2-Theta(°)
2T=3.790
2T=7.510
2T=8.190
2T=9.830
2T=11.410
2T=15.929
2T=16.451
2T=18.290
2T=19.191
2T=19.870
2T=20.630
2T=21.130
2T=22.010
2T=25.090
2T=26.450
2T=27.590
2T=28.130
2T=31.072

FIGURE 51

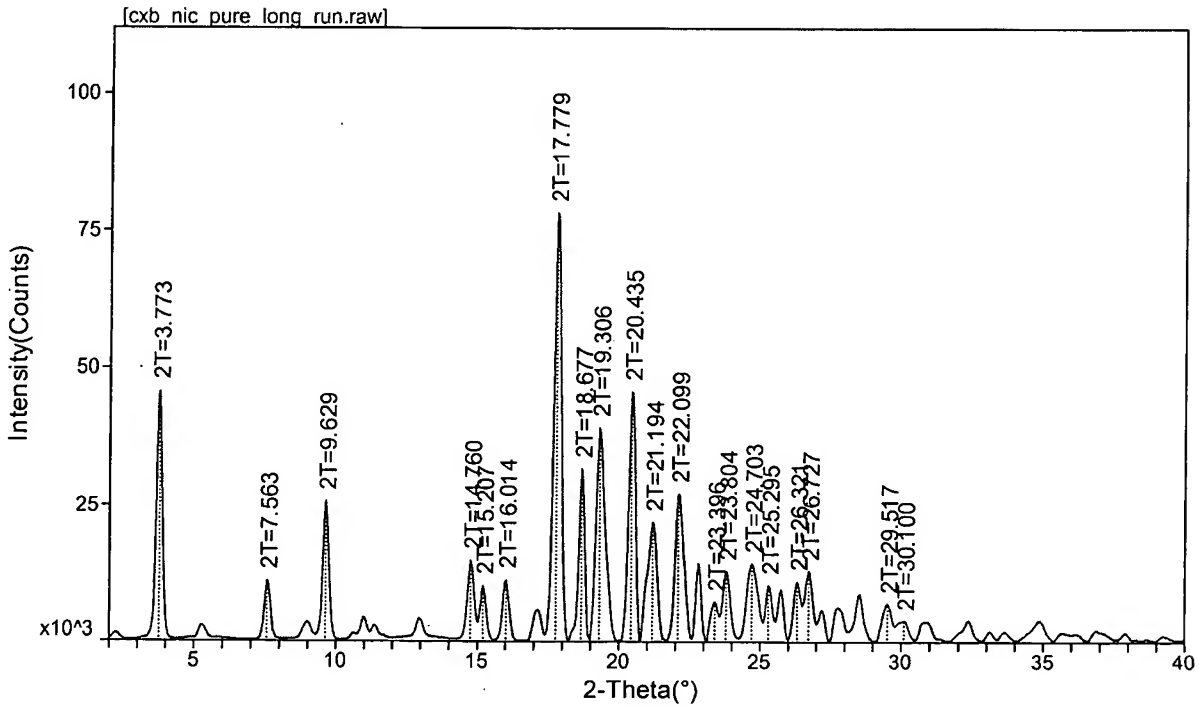

[cxb_nic_pure_long_run.raw]
Intensity(Counts)
x10^3
2-Theta(°)
2T=3.773
2T=7.563
2T=9.629
2T=14.760
2T=15.207
2T=16.014
2T=17.779
2T=18.677
2T=19.306
2T=20.435
2T=21.194
2T=22.099
2T=23.386
2T=23.804
2T=24.703
2T=25.295
2T=26.321
2T=26.727
2T=29.517
2T=30.100

FIGURE 52

17% RH

Celecoxib Na hydrate

Batch No. MT_138_A

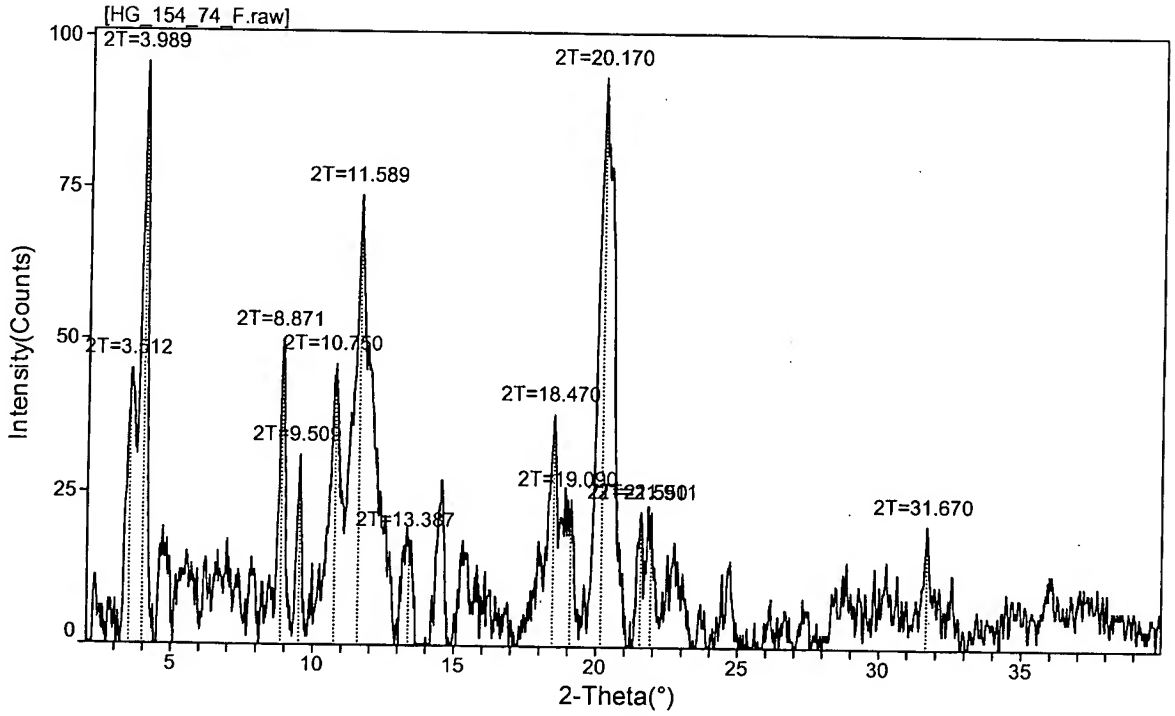


Figure 53

31% RH

Celecoxib Na hydrate

Batch No. MT_143_138_A

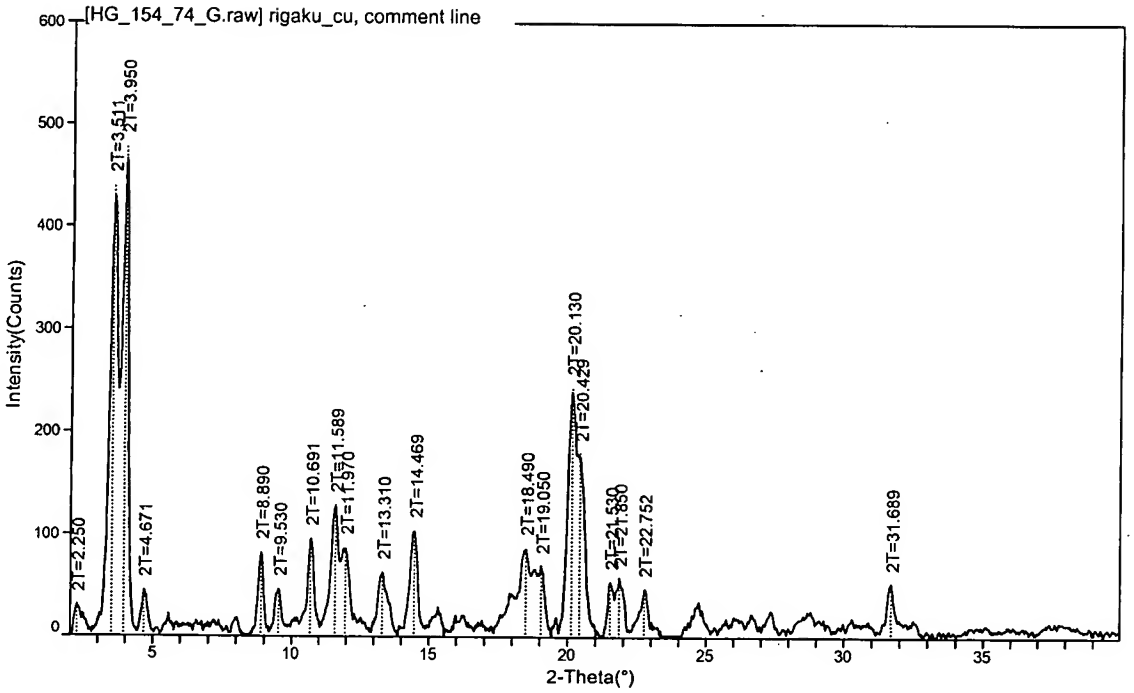


FIGURE 54

59% RH

Celecoxib Na hydrate

Batch No. MT_143_38_A

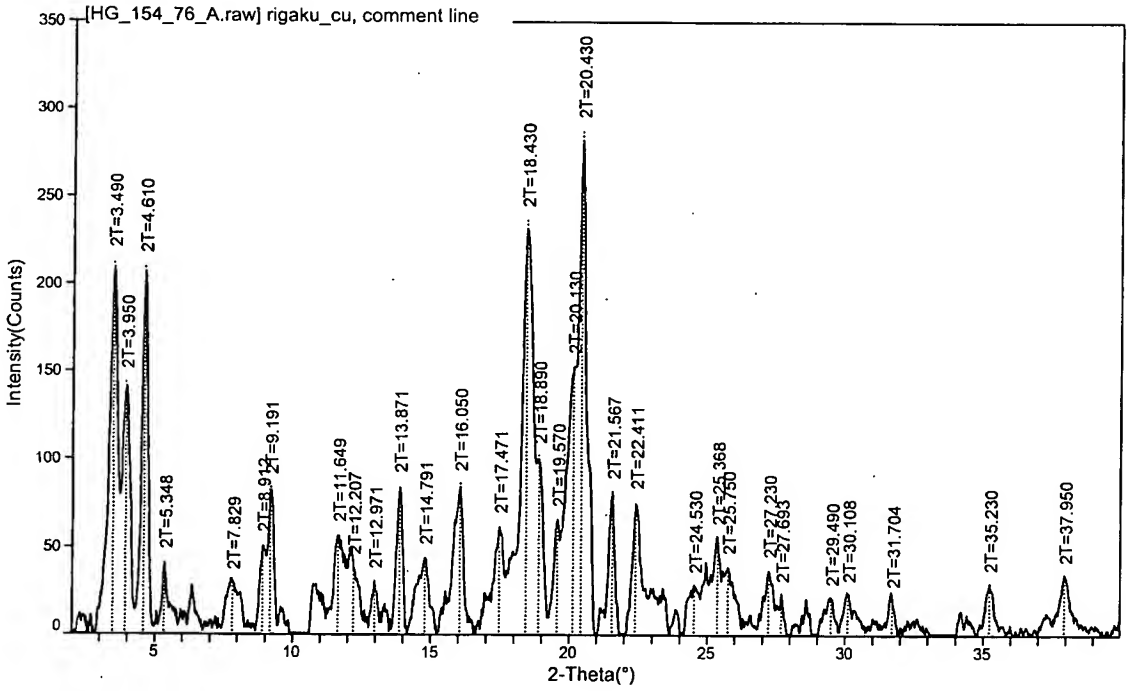


FIGURE 55

74% RH

Celecoxib Na hydrate

Batch No. MT_143_138_A

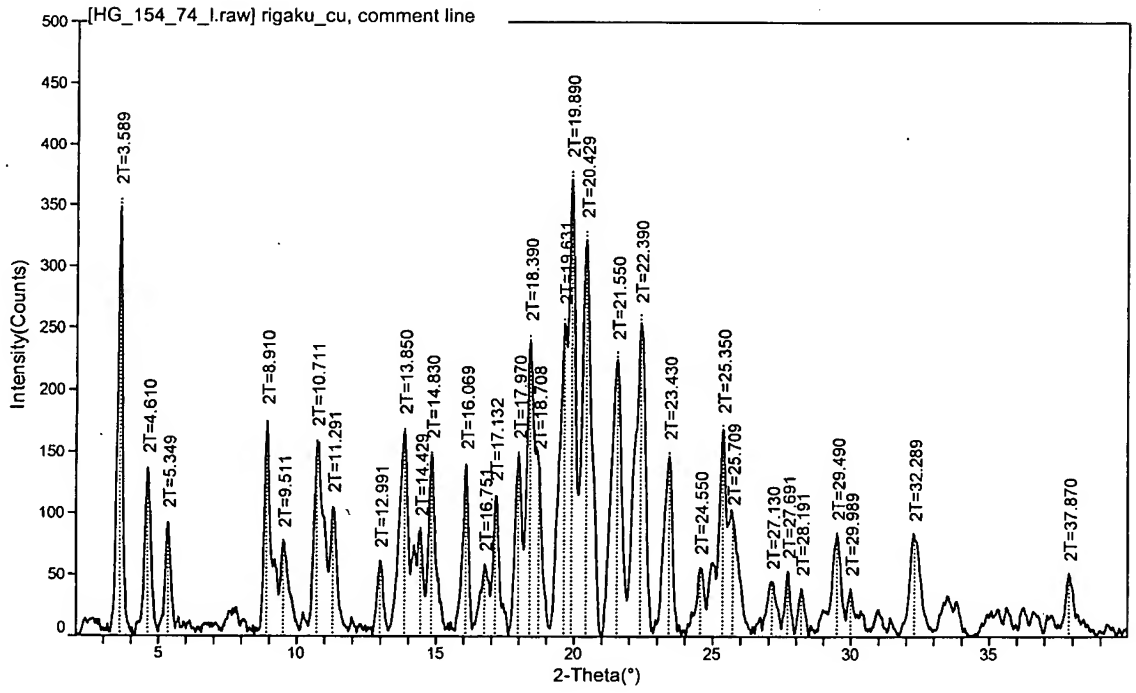


FIGURE 56

17% RH

Celecoxib Na propylene glycol solvate

Batch No. MT_143_25

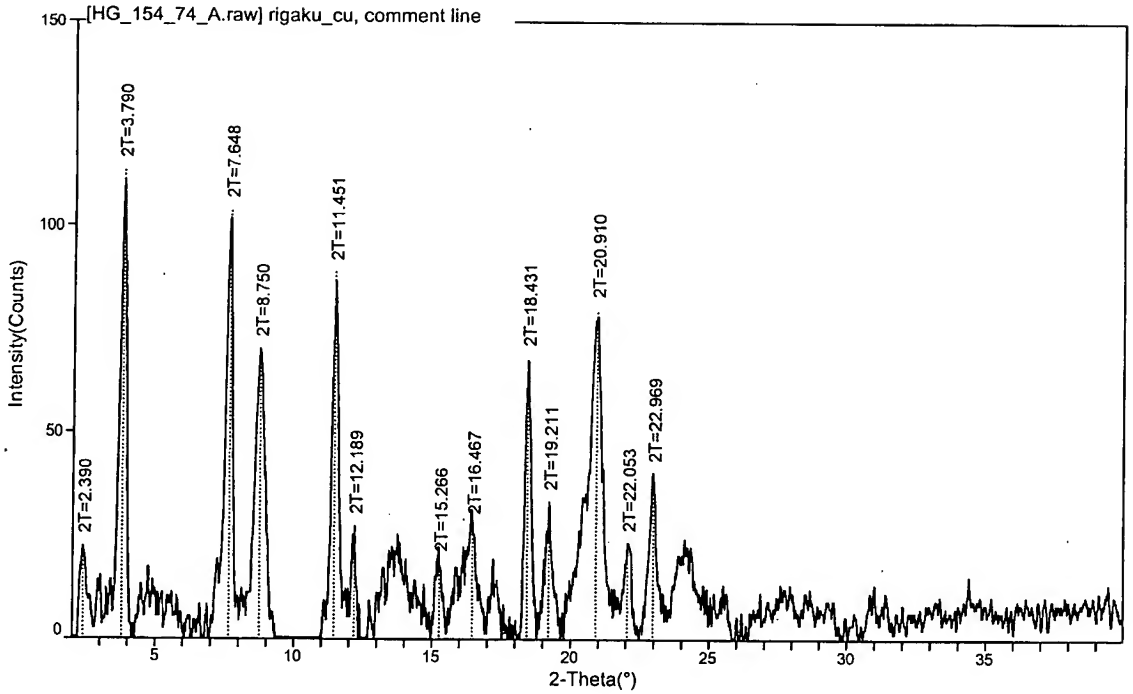


FIGURE 57

31% RH

Celecoxib Na propylene glycol solvate

Batch No. MT_143_25

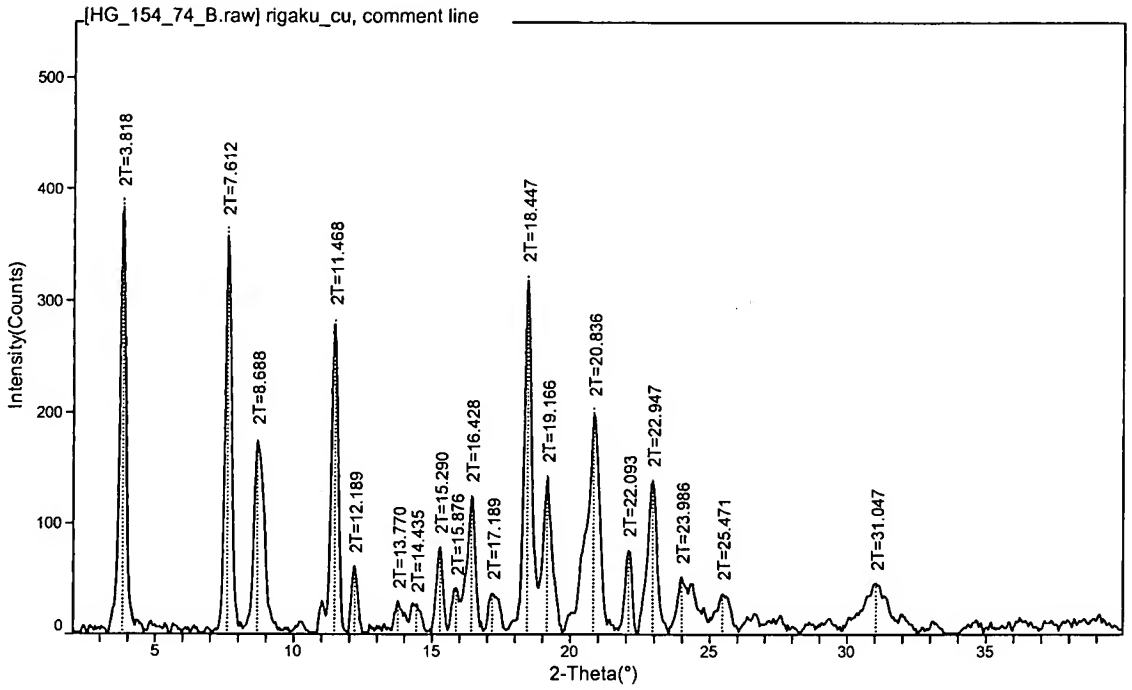


FIGURE 58

59% RH

Celecoxib Na propylene glycol solvate

Batch No. MT_143_25

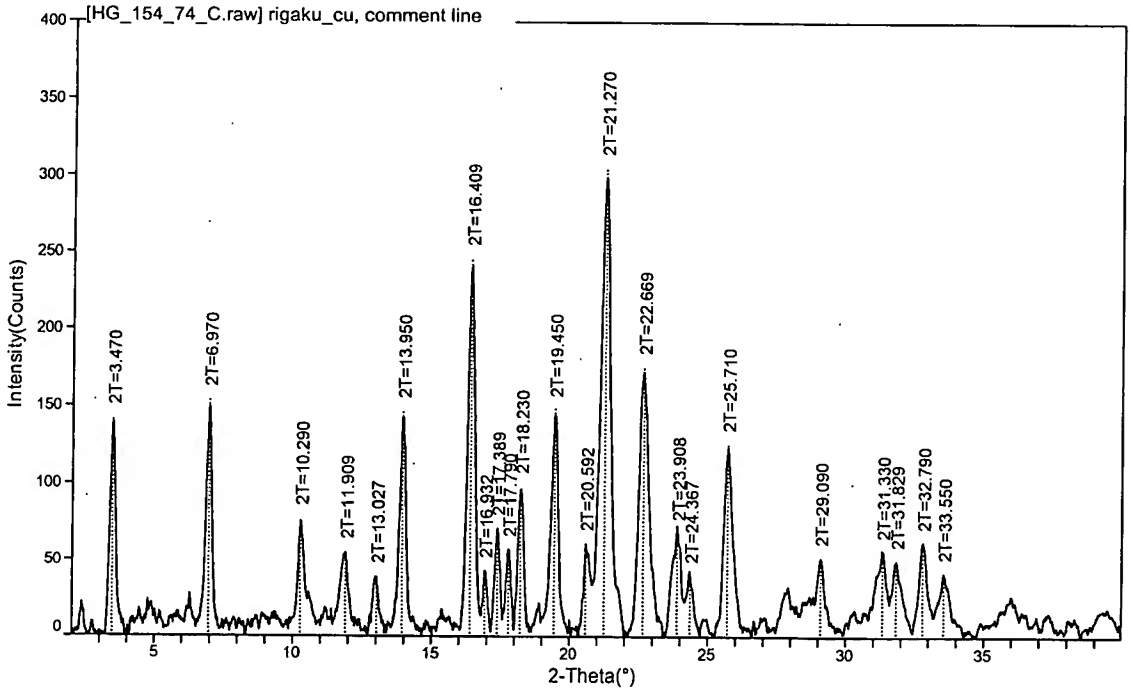


FIGURE 59

74% RH

Celecoxib Na propylene glycol solvate

Batch No. MT_143_25

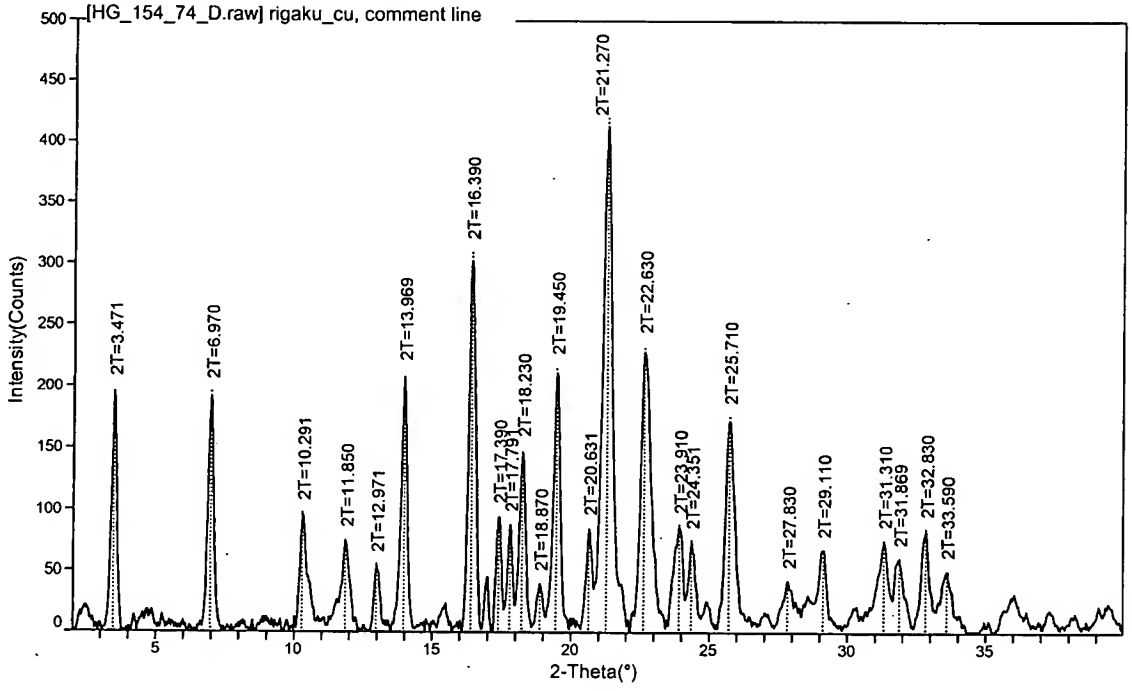


FIGURE 60

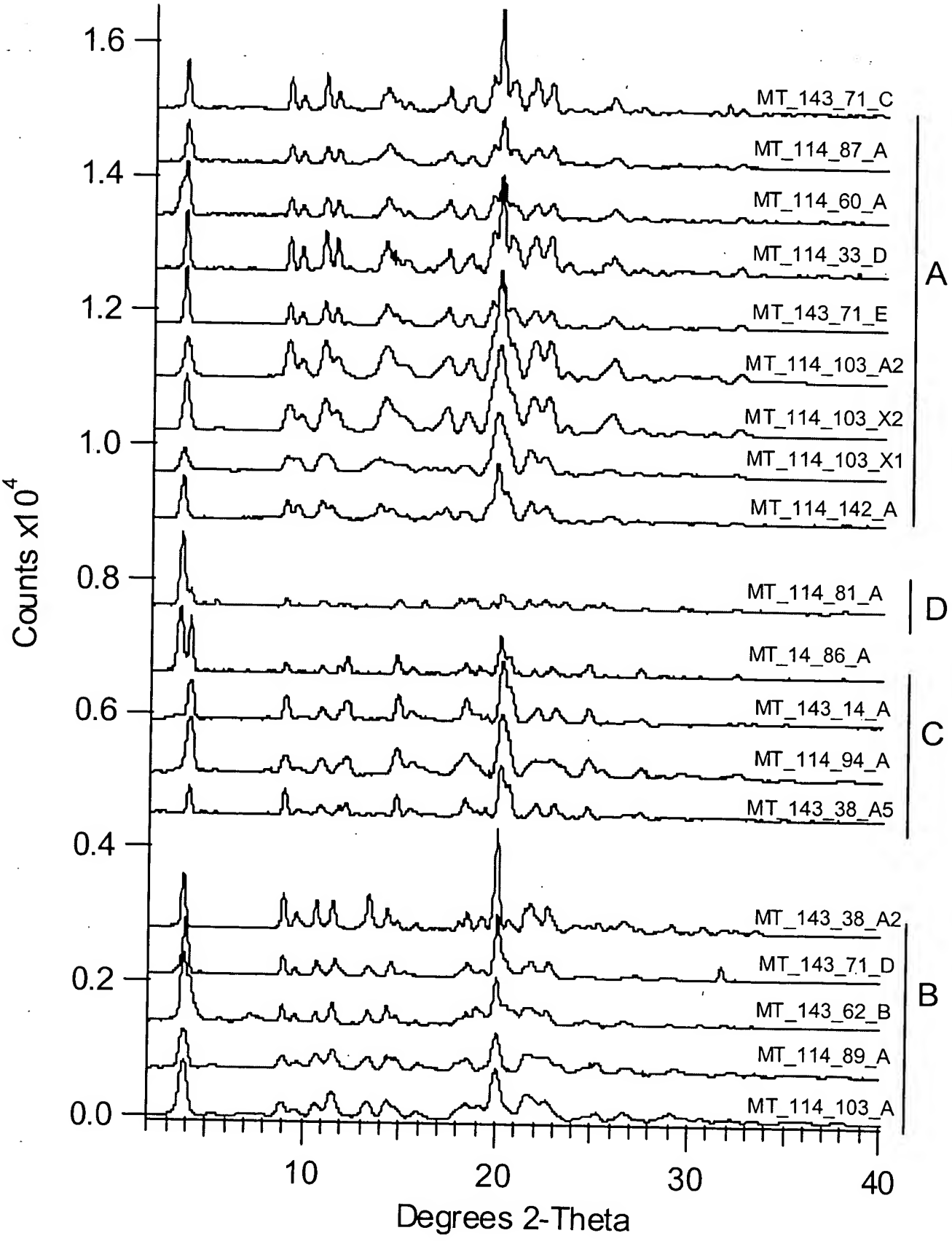

1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Counts x10^4
MT_143_71_C
MT_114_87_A
MT_114_60_A
MT_114_33_D
MT_143_71_E
MT_114_103_A2
MT_114_103_X2
MT_114_103_X1
MT_114_142_A
A
MT_114_81_A
MT_14_86_A
D
MT_143_14_A
MT_114_94_A
MT_143_38_A5
C
MT_143_38_A2
MT_143_71_D
MT_143_62_B
MT_114_89_A
MT_114_103_A
B
10
20
30
40
Degrees 2-Theta

Figure 61

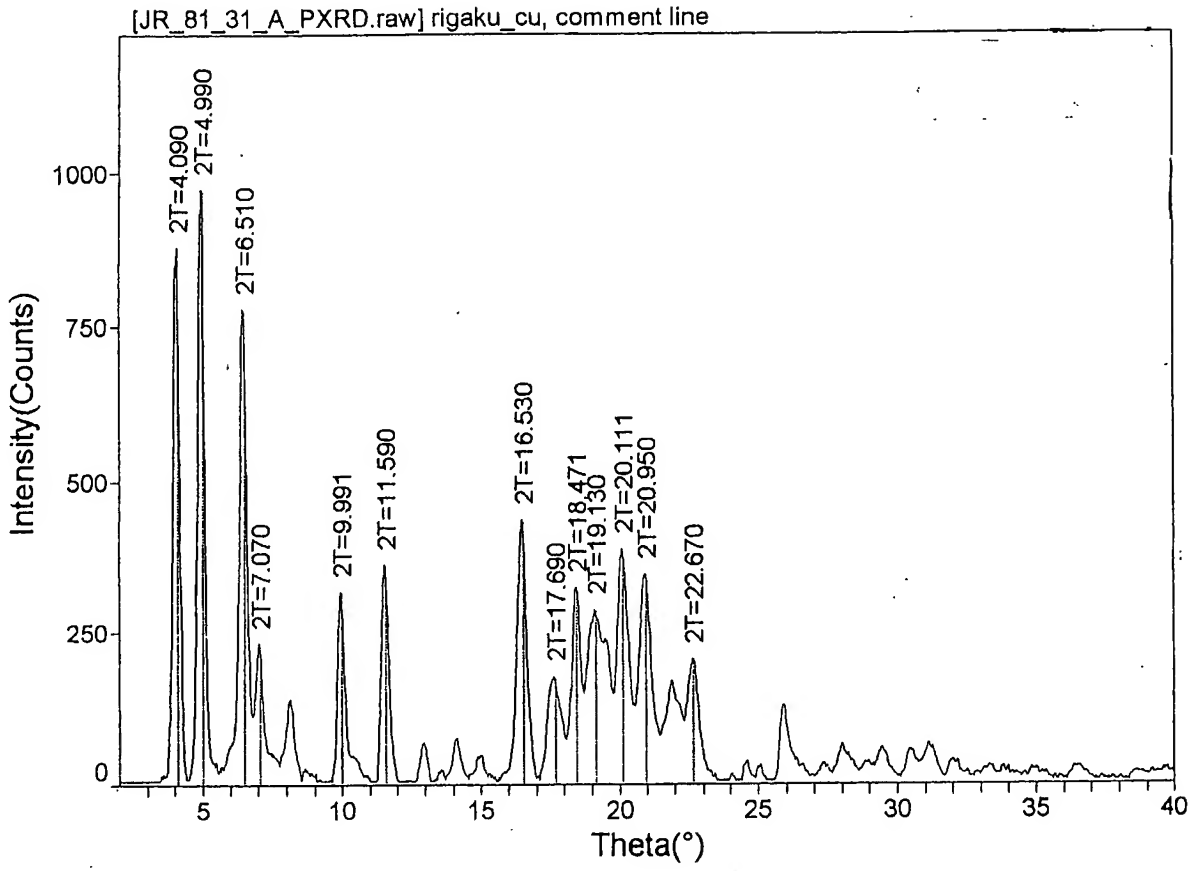

[JR_81_31_A_PXRD.raw] rigaku_cu, comment line
Intensity(Counts)
Theta(°)
2T=4.090
2T=4.990
2T=6.510
2T=7.070
2T=9.991
2T=11.590
2T=16.530
2T=17.690
2T=18.471
2T=19.130
2T=20.111
2T=20.950
2T=22.670

FIGURE 62